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(54) Title: GLUCOCORTICOID-SELECTIVE ANTIINFLAMMATORY AGENTS

(57) Abstract: Compounds having Formula I are useful for partially or fully antagonizing, repressing, agonizing, or modulating the glucocorticoid receptor and treating immune, autoimmune and inflammatory diseases in a mammal. Also disclosed are pharmaceutical compositions comprising compounds of Formula I and methods of inhibiting immune or autoimmune diseases in a mammal.

GLUCOCORTICOID-SELECTIVE ANTIINFLAMMATORY AGENTSTechnical Field

The present invention relates to glucocorticoid receptor-selective benzopyrano[3,4-f]quinolines that are useful for treating immune or autoimmune diseases, to pharmaceutical compositions comprising these compounds, and to methods of inhibiting inflammation, inflammatory disease, immune, and autoimmune diseases in a mammal.

Background of The Invention

Intracellular receptors (IR's) are a class of structurally related proteins involved in the regulation of gene expression. The steroid hormone receptors are a subset of this superfamily whose natural ligands are typically comprised of endogenous steroids such as estradiol, progesterone, and cortisol. Man-made ligands to these receptors play an important role in human health and, of these receptors, the glucocorticoid receptor (GR) has an essential role in regulating human physiology and immune response. Steroids which interact with GR have been shown to be potent antiinflammatory agents. Despite this benefit, steroidal GR ligands are not selective. Side effects associated with chronic dosing are believed to be the result of cross-reactivity with other steroid receptors such as estrogen, progesterone, androgen, and mineralocorticoid receptors which have somewhat homologous ligand binding domains.

Selective GR modulators (e.g. repressors, agonists, partial agonists and antagonists) of the present disclosure can be used to influence the basic, life-sustaining systems of the body, including carbohydrate, protein and lipid metabolism, and the functions of the cardiovascular, kidney, central nervous, immune, skeletal muscle, and other organ and tissue systems. In this regard, prior art GR modulators have proven useful in the treatment of inflammation, tissue rejection, auto-immunity, various malignancies, such as leukemias and lymphomas, Cushing's syndrome, acute adrenal insufficiency, congenital adrenal hyperplasia, rheumatic fever, polyarteritis nodosa, granulomatous polyarteritis, inhibition of myeloid cell lines, immune proliferation/apoptosis, HPA axis suppression and regulation, hypercortisolemia, modulation of the Th1/Th2 cytokine balance, chronic kidney disease, stroke and spinal cord injury, hypercalcemia, hyperglycemia, acute adrenal insufficiency, chronic primary adrenal insufficiency, secondary adrenal insufficiency, congenital adrenal hyperplasia, cerebral edema, thrombocytopenia, and Little's syndrome.

GR modulators are especially useful in disease states involving systemic inflammation such as inflammatory bowel disease, systemic lupus erythematosus, polyarthritis nodosa, Wegener's granulomatosis, giant cell arteritis, rheumatoid arthritis, osteoarthritis, hay fever, allergic rhinitis, urticaria, angioneurotic edema, chronic obstructive pulmonary disease, asthma,

tendonitis, bursitis, Crohn's disease, ulcerative colitis, autoimmune chronic active hepatitis, organ transplantation, hepatitis, and cirrhosis. GR active compounds have also been used as immunostimulants and repressors, and as wound healing and tissue repair agents.

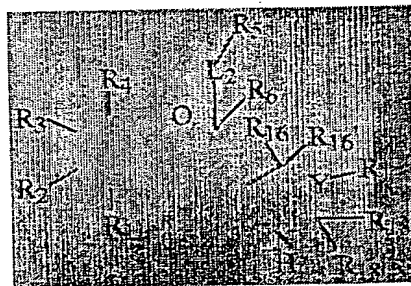
GR modulators have also found use in a variety of topical diseases such as inflammatory scalp alopecia, panniculitis, psoriasis, discoid lupus erythematosus, inflamed cysts, atopic dermatitis, pyoderma gangrenosum, pemphigus vulgaris, bullous pemphigoid, systemic lupus erythematosus, dermatomyositis, herpes gestationis, eosinophilic fasciitis, relapsing polychondritis, inflammatory vasculitis, sarcoidosis, Sweet's disease, type 1 reactive leprosy, capillary hemangiomas, contact dermatitis, atopic dermatitis, lichen planus, exfoliative dermatitis, erythema nodosum, acne, hirsutism, toxic epidermal necrolysis, erythema multiform, cutaneous T-cell lymphoma.

Selective antagonists of the glucocorticoid receptor have been unsuccessfully pursued for decades. These agents would potentially find application in several disease states associated with Human Immunodeficiency Virus (HIV), cell apoptosis, and cancer including, but not limited to, Kaposi's sarcoma, immune system activation and modulation, desensitization of inflammatory responses, IL-1 expression, anti-retroviral therapy, natural killer cell development, lymphocytic leukemia, and treatment of retinitis pigmentosa. Cognitive and behavioral processes are also susceptible to glucocorticoid therapy where antagonists would potentially be useful in the treatment of processes such as cognitive performance, memory and learning enhancement, depression, addiction, mood disorders, chronic fatigue syndrome, schizophrenia, stroke, sleep disorders, and anxiety.

### Summary of The Invention

In one embodiment of the present invention are compounds represented by

Formula I



I,

or a pharmaceutically acceptable salt or prodrug thereof, where

**R<sub>1</sub>** is -L<sub>1</sub>-R<sub>A</sub> where L<sub>1</sub> is selected from

- (1) a covalent bond,
- (2) -O-,
- (3) -S(O)<sub>t</sub>- where t is 0, 1, or 2,
- (4) -C(X)-,

(5) -NR<sub>7</sub>- where R<sub>7</sub> is selected from

- (a) hydrogen,
- (b) aryl
- (c) cycloalkyl of three to twelve carbons,
- (d) alkanoyl where the alkyl part is one to twelve carbons,
- (e) alkoxy carbonyl where the alkyl part is one to twelve carbons,
- (f) alkoxy carbonyl where the alkyl part is one to twelve carbons and is substituted by 1 or 2 aryl groups,
- (g) alkyl of one to twelve carbons,
- (h) alkyl of one to twelve carbons substituted with 1 or 2 substituents independently selected from
  - (i) aryl and
  - (ii) cycloalkyl of three to twelve carbons,
- (i) alkenyl of three to twelve carbons, provided that a carbon of a carbon-carbon double bond is not attached directly to nitrogen,
- (j) alkynyl of three to twelve carbons, provided that a carbon of a carbon-carbon triple bond is not attached directly to nitrogen,

(6) -NR<sub>8</sub>C(X)NR<sub>9</sub>- where X is O or S and R<sub>8</sub> and R<sub>9</sub> are independently selected from

- (a) hydrogen,
- (b) aryl,
- (c) cycloalkyl of three to twelve carbons,
- (d) alkyl of one to twelve carbons,
- (e) alkyl of one to twelve carbons substituted with 1 or 2 substituents independently selected from aryl or cycloalkyl of three to twelve carbons,
- (f) alkenyl of three to twelve carbons, provided that a carbon of a carbon-carbon double bond is not attached directly to nitrogen,
- (g) alkynyl of three to twelve carbons, provided that a carbon of a carbon-carbon triple bond is not attached directly to nitrogen,

(7) -X'C(X)- where X is previously defined and X' is O or S,

(8) -C(X)X'-,

(9) -X'C(X)X''- where X and X' are previously defined and X'' is O or S,

provided that when X is O, at least one of X' or X'' is O,

- (10)  $-\text{NR}_8\text{C}(\text{X})-$ ,
- (11)  $-\text{C}(\text{X})\text{NR}_8-$ ,
- (12)  $-\text{NR}_8\text{C}(\text{X})\text{X}'-$ ,
- (13)  $-\text{X}'\text{C}(\text{X})\text{NR}_8-$ ,
- 5 (14)  $-\text{SO}_2\text{NR}_8-$ ,
- (15)  $-\text{NR}_8\text{SO}_2-$ , and
- (16)  $-\text{NR}_8\text{SO}_2\text{NR}_9-$

where (6)-(16) are drawn with their right ends attached to  $\text{R}_\text{A}$  and  $\text{R}_\text{A}$  is selected from

- 10 (1)  $-\text{OH}$ ,
- (2)  $-\text{OG}$  where G is a  $-\text{OH}$  protecting group,
- (3)  $-\text{SH}$ ,
- (4)  $-\text{CO}_2\text{R}_{20}$  where  $\text{R}_{20}$  is hydrogen or alkyl of one to twelve carbons,
- (5) alkoxy carbonyl,
- 15 (6)  $-\text{CN}$ ,
- (7) halo,
- (8) haloalkoxy of one to twelve carbons,
- (9) perfluoroalkoxy of one to twelve carbons,
- (10)  $-\text{CHO}$ ,
- 20 (11)  $-\text{NR}_7\text{R}_{7'}$  where  $\text{R}_7$  is defined previously and  $\text{R}_{7'}$  is selected from
  - (a) hydrogen,
  - (b) aryl,
  - (c) cycloalkyl of three to twelve carbons,
  - (d) alkanoyl where the alkyl part is one to twelve carbons,
  - 25 (e) alkoxy carbonyl where the alkyl part is one to twelve carbons,
  - (f) alkoxy carbonyl where the alkyl part is one to twelve carbons and is substituted by 1 or 2 aryl groups,
  - (g) alkyl of one to twelve carbons,
  - (h) alkyl of one to twelve carbons substituted with 1 or 2 substituents independently selected from
    - 30 (i) aryl and
    - (ii) cycloalkyl of three to twelve carbons,
    - (i) alkenyl of three to twelve carbons, provided that a carbon of a carbon-carbon double bond is not attached directly to nitrogen,
    - 35 (j) alkynyl of three to twelve carbons, provided that a carbon of a carbon-carbon triple bond is not attached directly to nitrogen,

(12)  $-C(X)NR_8R_9$ ,

(13)  $-OSO_2R_{11}$  where  $R_{11}$  is selected from

(a) aryl,

(b) cycloalkyl of three to twelve carbons,

(c) alkyl of one to twelve carbons,

(d) alkyl of one to twelve carbons substituted with 1, 2, 3, or 4 halo substituents, and

(e) perfluoroalkyl of one to twelve carbons,

(14) alkyl of one to twelve carbons,

(15) alkenyl of two to twelve carbons,

provided that a carbon of a carbon-carbon double bond is not attached directly to  $L_1$  when  $L_1$  is other than a covalent bond,

(16) alkynyl of two to twelve carbons,

provided that a carbon of a carbon-carbon triple bond is not attached directly to  $L_1$  when  $L_1$  is other than a covalent bond,

where (14), (15), and (16) can be optionally substituted with 1, 2, or 3 substituents independently selected from

(a) alkoxy of one to twelve carbons,

(b)  $-OH$ ,

provided that no two  $-OH$  groups are attached to the same carbon,

(c)  $-SH$ ,

(d) thioalkoxy of one to twelve carbons,

provided that no two  $-SH$  groups are attached to the same carbon,

(e)  $-CN$ ,

(f) halo,

(g)  $-CHO$ ,

(h)  $-NO_2$ ,

(i) haloalkoxy of one to twelve carbons,

(j) perfluoroalkoxy of one to twelve carbons,

(k)  $-NR_7R_7'$ ,

(l)  $=NNR_7R_7'$ ,

(m)  $-NR_7NR_7'R_7''$  where  $R_7$  and  $R_7'$  are defined previously and  $R_7''$  is selected from

(i) hydrogen,

(ii) aryl,

(iii) cycloalkyl of three to twelve carbons,

(vi) alkanoyl where the alkyl part is one to twelve carbons,

(v) alkoxycarbonyl where the alkyl part is one to twelve carbons,

- (vi) alkoxy carbonyl where the alkyl part is one to twelve carbons substituted by 1 or 2 aryl groups,
- (vii) alkyl of one to twelve carbons,
- (viii) alkyl of one to twelve carbons substituted with 1 or 2 substituents independently selected from aryl or cycloalkyl of three to twelve carbons,
- (ix) alkenyl of three to twelve carbons, provided that a carbon-carbon double bond is not attached directly to nitrogen, and
- (x) alkynyl of three to twelve carbons, provided that a carbon-carbon triple bond is not attached directly to nitrogen,
- (n)  $-\text{CO}_2\text{R}_{10}$  where  $\text{R}_{10}$  is selected from
- (i) aryl,
- (ii) aryl substituted with 1, 2, or 3 alkyl of one to twelve carbon substituents,
- (ii) cycloalkyl of three to twelve carbons,
- (iii) alkyl of one to twelve carbons, and
- (iv) alkyl of one to twelve carbons substituted with aryl or cycloalkyl of three to twelve carbons,
- (o)  $-\text{C}(\text{X})\text{NR}_8\text{R}_9$ ,
- (p)  $=\text{N}-\text{OR}_{10}$ ,
- (q)  $=\text{NR}_{10}$ ,
- (r)  $-\text{S}(\text{O})_t\text{R}_{10}$ ,
- (s)  $-\text{X}'\text{C}(\text{X})\text{R}_{10}$ ,
- (t)  $(=\text{X})$ , and
- (u)  $-\text{OSO}_2\text{R}_{11}$ ,
- (17) cycloalkyl of three to twelve carbons,
- (18) cycloalkenyl of four to twelve carbons, provided that a carbon of a carbon-carbon double bond is not attached directly to  $\text{L}_1$  when  $\text{L}_1$  is other than a covalent bond,
- where (17) and (18) can be optionally substituted with 1, 2, 3, or 4 substituents independently selected from
- (a) alkyl of one to twelve carbons,
- (b) aryl,
- (c) alkoxy of one to twelve carbons,
- (d) halo,
- (e) alkoxy carbonyl where the alkyl group is one to twelve carbons, and

(f) -OH,  
provided that no two -OH groups are attached to the same carbon,

(19) perfluoroalkyl of one to twelve carbons,

(20) aryl, and

(21) heterocycle

where (20) and (21) can be optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from

(a) alkyl of one to twelve carbons,

(b) alkanoyloxy where the alkyl part is one to twelve carbons,

(c) alkoxy carbonyl where the alkyl part is one to twelve carbons,

(d) alkoxy of one to twelve carbons,

(e) halo,

(f) -OH,

provided that no two -OH groups are attached to the same carbon,

(g) thioalkoxy of one to twelve carbons,

(h) perfluoroalkyl of one to twelve carbons,

(i) -NR<sub>7</sub>R<sub>7'</sub>,

(j) -CO<sub>2</sub>R<sub>10</sub>,

(k) -OSO<sub>2</sub>R<sub>11</sub>, and

(l) (=X);

**R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub>** are independently hydrogen or R<sub>1</sub>; or

**R<sub>1</sub> and R<sub>2</sub>** together are -X\*-Y\*-Z\*- where X\* is -O- or -CH<sub>2</sub>-, Y\* is -C(O)- or -(C(R<sub>12</sub>)(R<sub>13</sub>))<sub>v</sub> - where R<sub>12</sub> and R<sub>13</sub> are independently hydrogen or alkyl of one to twelve carbons and v is 1, 2, or 3, and Z\* is selected from -CH<sub>2</sub>-, -CH<sub>2</sub>S(O)<sub>t</sub>-, -CH<sub>2</sub>O-, -CH<sub>2</sub>NR<sub>7</sub>-, -NR<sub>7</sub>-, and -O-;

**L<sub>2</sub>** is selected from

(1) a covalent bond,

(2) alkylene of one to twelve carbons,

(3) alkylene of one to twelve carbons substituted with 1 or 2 substituents independently selected from

(a) spiroalkyl of three to eight carbon atoms,

(b) spiroalkenyl of five or eight carbon atoms,

(c) oxo,

(d) halo, and

(e) -OH,

provided that no two -OH groups are attached to the same carbon,

(4) alkynylene of two to twelve carbons,

(5) -NR<sub>7</sub>-,

(6) -C(X)-,

(7) -O-, and

(8) -S(O)<sub>t</sub>-; and

R<sub>5</sub> is selected from

(1) halo,

(2) hydrogen,

(3) -C(=NR<sub>7</sub>)OR<sub>10</sub>,

(4) -CN,

provided that when R<sub>5</sub> is (1), (2), or (3), L<sub>2</sub> is a covalent bond,

(5) alkyl of one to twelve carbons,

(6) alkynyl two to twelve carbons,

provided that a carbon of a carbon-carbon triple bond is not attached directly to L<sub>3</sub> when L<sub>3</sub> is other than a covalent bond,

(7) cycloalkyl of three to twelve carbons,

(8) heterocycle,

(9) aryl

where (5)-(9) can be optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from

(a) -OH,

provided that no two -OH groups are attached to the same carbon,

(b) -SH,

provided that no two -SH groups are attached to the same carbon,

(c) -CN,

(d) halo,

(e) -CHO,

(f) -NO<sub>2</sub>,

(g) haloalkoxy of one to twelve carbons,

(h) perfluoroalkoxy of one to twelve carbons,

(i) -NR<sub>8</sub>R<sub>9</sub>' where R<sub>8</sub>' and R<sub>9</sub>' are selected from

(i) hydrogen,

(ii) alkanoyl where the alkyl part is one to twelve carbons,

(iii) alkoxycarbonyl where the alkyl part is one to twelve carbons,

(iv) alkoxycarbonyl where the alkyl part is one to twelve carbons

and is substituted with 1 or 2 phenyl substituents,

- (v) cycloalkyl of three to twelve carbons,  
(vi) alkyl of one to twelve carbons,  
(vii) alkyl of one to twelve carbons substituted with 1, 2, or 3  
5 substituents independently selected from  
alkoxy of one to twelve carbons,  
cycloalkyl of three to twelve carbons,  
aryl, and  
alkoxycarbonyl where the alkyl group is one to twelve  
10 carbons,  
(viii) alkenyl of three to twelve carbons,  
provided that a carbon of a carbon-carbon double bond is  
not directly attached to nitrogen,  
(ix) alkynyl of three to twelve carbons,  
15 provided that a carbon of a carbon-carbon triple bond is not  
directly attached to nitrogen,  
(x) -C(O)NR<sub>X</sub>R<sub>Y</sub> where R<sub>X</sub> and R<sub>Y</sub> are independently selected  
from hydrogen and alkyl of one to twelve carbons,  
(xi) alkoxy of one to twelve carbons,  
20 (xii) aryl, and  
(xiii) aryl substituted with 1, 2, 3, 4, or 5 substituents  
independently selected from  
alkyl of one to twelve carbons,  
alkanoyloxy where the alkyl part is one to twelve carbons,  
25 alkoxycarbonyl where the alkyl part is one to twelve carbons,  
alkoxy of one to twelve carbons,  
halo,  
-OH  
provided that no two -OH groups are attached to the same  
30 carbon,  
thioalkoxy of one to twelve carbons,  
perfluoroalkyl of one to twelve carbons,  
-NR<sub>7</sub>R<sub>7'</sub>,  
-CO<sub>2</sub>R<sub>10</sub>,  
35 -OSO<sub>2</sub>R<sub>11</sub>, and  
(=X), or

R<sub>8</sub>' and R<sub>9</sub>' together with the nitrogen atom to which they are  
attached form a ring selected from

- (i) aziridine,
- (ii) azetidine,
- (iii) pyrrolidine,
- (iv) piperidine,
- (v) pyrazine,
- (vi) morpholine,
- (vii) phthalimide,
- (viii) thiomorpholine, and
- (ix) thiomorpholine sulfone

where (i)-(ix) can be optionally substituted with 1, 2, or 3 alkyl of one to twelve carbon substituents,

- (j) =NNR<sub>8</sub>R<sub>9</sub>,
- (k) -NR<sub>7</sub>NR<sub>8</sub>R<sub>9</sub>,
- (l) -CO<sub>2</sub>R<sub>8</sub>,
- (m) -C(X)NR<sub>8</sub>R<sub>9</sub>,
- (n) =N-OR<sub>8</sub>,
- (o) =NR<sub>8</sub>,
- (p) -S(O)<sub>t</sub>R<sub>10</sub>,
- (q) -X'C(X)R<sub>8</sub>,
- (r) (=X),
- (s) -O-(CH<sub>2</sub>)<sub>q</sub>-Z-R<sub>10</sub> where R<sub>10</sub> is defined previously, q is 1, 2, or 3, and Z is O or -S(O)<sub>t</sub>,
- (t) -OC(X)NR<sub>8</sub>R<sub>9</sub>,
- (u) -OSO<sub>2</sub>R<sub>11</sub>,
- (v) alkanoyloxy where the alkyl group is one to twelve carbons,
- (w) -LB R<sub>30</sub> where LB is selected from
  - (i) a covalent bond,
  - (ii) -O-,
  - (iii) -S(O)<sub>t</sub>-, and
  - (iv) -C(X)- and
 R<sub>30</sub> is selected from
  - (i) alkyl of one to twelve carbons,
  - (ii) alkenyl of one to twelve carbons,  
provided that a carbon of a carbon-carbon double bond is not attached directly to LB when LB is other than a covalent bond,
  - (iii) alkynyl of one to twelve carbons,  
provided that a carbon of a carbon-carbon triple bond is not attached directly to LB when LB is other than a covalent bond,

where (i), (ii), and (iii) can be optionally substituted with

cycloalkyl of three to twelve carbons,

-OH,

provided that no two -OH groups are attached to the same

carbon,

halo,

alkoxy of one to twelve carbons,

thioalkoxy of one to twelve carbons,

-NR<sub>8</sub>R<sub>9</sub>,

-O-(CH<sub>2</sub>)<sub>q</sub>-Z-R<sub>10</sub>,

alkoxycarbonyl where the alkyl group is one to twelve carbons,

alkanoyloxy where the alkyl group is one to twelve carbons,

-NR<sub>7</sub>SO<sub>2</sub>-(alkyl of one to twelve carbons),

-OSO<sub>2</sub>-(alkyl of one to twelve carbons),

aryl, and

heterocycle,

(iv) aryl,

(v) aryl substituted with 1, 2, 3, 4, or 5 substituents independently selected from

alkyl of one to twelve carbons,

halo,

-NO<sub>2</sub>, and

-OH,

provided that no two -OH groups are attached to the same carbon,

(vi) heterocycle, and

(vii) heterocycle substituted with 1, 2, 3, 4, or 5 substituents independently selected from

alkyl of one to twelve carbons,

halo,

-NO<sub>2</sub>, and

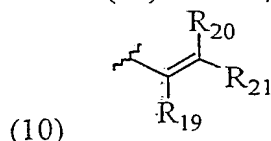
-OH,

provided that no two -OH groups are attached to the same carbon,

(x) -X'C(X)X"R<sub>10</sub>,

(y) -NHC(O)NHNH<sub>2</sub>,

- (z) alkenyl of two carbons,
- (aa)  $-C(=NR_7)OR_{10}$ , and
- (bb)  $-NR_7(X)NR_8'R_9'$ ,



provided that when  $R_5$  is (9),  $L_3$  is other than  $-NR_7-$  or  $-O-$ , where the carbon-carbon double bond is in the Z or E configuration, and  $R_{19}$ ,  $R_{20}$ , and  $R_{21}$  are independently selected from

- (a) hydrogen,
- (b) halo,
- (c) alkoxycarbonyl where the alkyl group is of one to twelve carbons,
- (d) alkyl of one to twelve carbons, and
- (e) alkyl of one to twelve carbons substituted with
  - (i) alkoxy of one to twelve carbons,
  - (ii)  $-OH$ ,  
provided that no two  $-OH$  groups are attached to the same carbon,
  - (iii)  $-SH$ ,  
provided that no two  $-SH$  groups are attached to the same carbon,
  - (iv)  $-CN$ ,
  - (v) halo,
  - (vi)  $-CHO$ ,
  - (vii)  $-NO_2$ ,
  - (viii) haloalkoxy of one to twelve carbons,
  - (ix) perfluoroalkoxy of one to twelve carbons,
  - (x)  $-NR_8'R_9'$
  - (xi)  $=NNR_8'R_9'$ ,
  - (xii)  $-NR_7NR_8'R_9'$ ,
  - (xiii)  $-CO_2R_{10}$ ,
  - (xiv)  $-C(X)NR_8'R_9'$ ,
  - (xv)  $=N-OR_{10}$ ,
  - (xvi)  $=NR_{10}$ ,
  - (xvii)  $-S(O)_tR_{10}$ ,
  - (xviii)  $-X'C(X)R_{10}$ ,
  - (xix)  $(=X)$ ,
  - (xx)  $-O-(CH_2)_q-Z-R_{10}$ ,

(xxi)  $-\text{OC}(\text{X})\text{NR}_8'\text{R}_9'$ ,

(xxii)  $-\text{LBR}_{30}$ ,

(xxiii) alkanoyloxy where the alkyl group is one to twelve carbons,

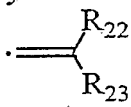
(xxiv)  $-\text{OSO}_2\text{R}_{11}$ , and

(xxv)  $-\text{NR}_7(\text{X})\text{NR}_8'\text{R}_9'$ , or

$\text{R}_{20}$  and  $\text{R}_{21}$  together are selected from

(a) cycloalkyl of three to twelve carbon atoms,

(b) cycloalkenyl of four to twelve carbon atoms, and

(c)  (allene) where  $\text{R}_{22}$  and  $\text{R}_{23}$  are independently

hydrogen or alkyl of one to twelve carbons, and

(11) cycloalkenyl of four to twelve carbons

where the cycloalkenyl group or the ring formed by  $\text{R}_{20}$  and  $\text{R}_{21}$  together can be optionally substituted with one or two substituents independently selected from

(a) alkoxy of one to twelve carbons,

(b)  $-\text{OH}$ ,

provided that no two  $-\text{OH}$  groups are attached to the same carbon,

(c)  $-\text{SH}$ ,

provided that no two  $-\text{SH}$  groups are attached to the same carbon,

(d)  $-\text{CN}$ ,

(e) halo,

(f)  $-\text{CHO}$ ,

(g)  $-\text{NO}_2$ ,

(h) haloalkoxy of one to twelve carbons,

(i) perfluoroalkoxy of one to twelve carbons,

(j)  $-\text{NR}_8'\text{R}_9'$

(k)  $=\text{NNR}_8'\text{R}_9'$ ,

(l)  $-\text{NR}_7\text{NR}_8'\text{R}_9'$ ,

(m)  $-\text{CO}_2\text{R}_{10}$ ,

(n)  $-\text{C}(\text{X})\text{NR}_8'\text{R}_9'$ ,

(o)  $=\text{N}-\text{OR}_{10}$ ,

(p)  $=\text{NR}_{10}$ ,

(q)  $-\text{S}(\text{O})_t\text{R}_{10}$ ,

(r)  $-\text{X}'\text{C}(\text{X})\text{R}_{10}$ ,

(s)  $(=\text{X})$ ,

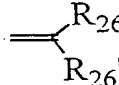
(t)  $-\text{O}-(\text{CH}_2)_q-\text{Z}-\text{R}_{10}$ ,

- (u)  $-\text{OC}(\text{X})\text{NR}_8'\text{R}_9'$ ,
- (v)  $-\text{LBR}_{30}$ ,
- (w) alkanoyloxy where the alkyl group is one to twelve carbons,
- (x)  $-\text{OSO}_2\text{R}_{11}$ , and
- (y)  $-\text{NR}_7(\text{X})\text{NR}_8'\text{R}_9'$ ;

$\text{R}_6$  is hydrogen or alkyl of one to twelve carbon atoms; or

$-\text{L}_2-\text{R}_5$  and  $\text{R}_6$  together are selected from

- (1)  $=\text{O}$ ,
- (2)  where  $\square$  is 1, 2, 3, or 4 and A is selected from
  - (a)  $-\text{CH}_2-$ ,
  - (b)  $-\text{O}-$ ,
  - (c)  $-\text{S}(\text{O})_t$ , and
  - (d)  $-\text{NR}_7-$ , and

- (3)  where the carbon-carbon double bond can be in the E or Z configuration and  $\text{R}_{26}$  and  $\text{R}_{26}'$  are independently selected from

- (a) hydrogen,
- (b) alkenyl of three to twelve carbons,
- (c) aryl,
- (d) heterocycle,
- (e) alkyl of one to twelve carbons,
- (f) cycloalkyl of three to twelve carbons,
- (g) cycloalkenyl of four to twelve carbons, and
- (h) cycloalkenyl of four to twelve carbons where (a)-(f) can be optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from
  - (i) alkoxy of one to twelve carbons,
  - (ii)  $-\text{OH}$ ,  
provided that no two  $-\text{OH}$  groups are attached to the same carbon,
  - (iii)  $-\text{SH}$ ,  
provided that no two  $-\text{SH}$  groups are attached to the same carbon,

- (iv) -CN,
- (v) halo,
- (vi) -CHO,
- (vii) -NO<sub>2</sub>,
- 5 (viii) haloalkoxy of one to twelve carbons,
- (ix) perfluoroalkoxy of one to twelve carbons,
- (x) -NR<sub>8</sub>'R<sub>9</sub>'
- (xi) =NNR<sub>8</sub>'R<sub>9</sub>'
- (xii) -NR<sub>7</sub>NR<sub>8</sub>'R<sub>9</sub>'
- 10 (xiii) -CO<sub>2</sub>R<sub>10</sub>,
- (xiv) -C(X)NR<sub>8</sub>'R<sub>9</sub>'
- (xv) =N-OR<sub>10</sub>,
- (xvi) =NR<sub>10</sub>,
- (xvii) -S(O)<sub>t</sub>R<sub>10</sub>,
- 15 (xviii) -X'C(X)R<sub>10</sub>,
- (xix) (=X),
- (xx) -O-(CH<sub>2</sub>)<sub>q</sub>-Z-R<sub>10</sub>,
- (xxi) -OC(X)NR<sub>8</sub>'R<sub>9</sub>'
- (xxii) -LB<sub>30</sub>,
- 20 (xxiii) alkanoyloxy where the alkyl group is one to twelve carbons,
- (xxiii) -OSO<sub>2</sub>R<sub>11</sub>, and
- (xxiv) -NR<sub>7</sub>(X)NR<sub>8</sub>'R<sub>9</sub>'

**R<sub>16</sub>** and **R<sub>16</sub>'** are independently hydrogen or alkyl of one to six carbons; or

**R<sub>16</sub>** and **R<sub>16</sub>'** together are alkenyl of two carbons;

a broken line represents the optional presence of a double bond,  
provided that when **R<sub>16</sub>** and **R<sub>16</sub>'** together are alkenyl of two carbons, the double  
bond is not present;

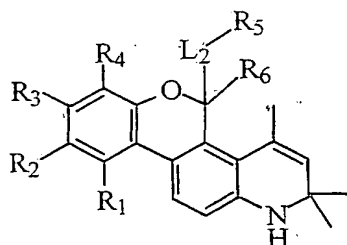
**Y** is selected from carbon, nitrogen, and N<sup>+</sup>(=O<sup>-</sup>);

**R<sub>17</sub>** is absent or hydrogen or alkyl of one to six carbons,  
provided that when the double bond is present, and **Y** is nitrogen or N<sup>+</sup>(=O<sup>-</sup>), **R<sub>17</sub>** is  
absent; and

**R<sub>18</sub>** and **R<sub>18</sub>'** are independently hydrogen or alkyl of one to six carbons; or  
**R<sub>18</sub>** and **R<sub>18</sub>'** together are a cycloheteroalkyl ring or a cycloalkyl ring of three to

eight carbons.

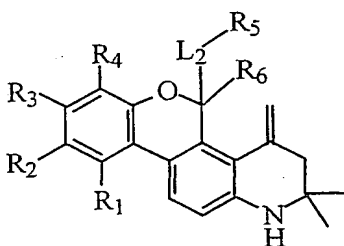
In another embodiment of the invention are disclosed compounds of Formula II



II,

or a pharmaceutically acceptable salt or prodrug thereof, where  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ ,  $R_6$ , and  $L_2$ , are defined above.

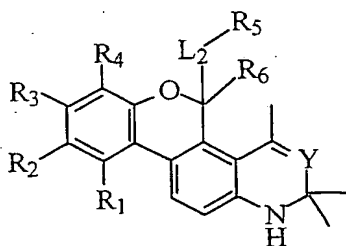
In another embodiment of the invention are disclosed compounds of Formula III



III,

or a pharmaceutically acceptable salt or prodrug thereof, where  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ ,  $R_6$ , and  $L_2$ , are defined above.

In another embodiment of the invention are disclosed compounds of Formula IV



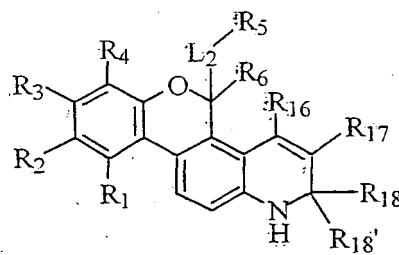
IV,

or a pharmaceutically acceptable salt or prodrug thereof, where

$Y$  is nitrogen or  $N^+(=O^-)$ , and

$R_1$ ,  $R_5$ ,  $R_6$ , and  $L_2$ , are defined above.

In another embodiment of the invention are disclosed compounds of Formula V


$$\mathbf{V}_n$$

or a pharmaceutically acceptable salt or prodrug thereof, where  $R_1$ ,  $R_5$ , and  $L_2$ , are defined above;

**R<sub>16</sub>** and **R<sub>17</sub>** are independently hydrogen or alkyl of one to six carbons; and

**R<sub>18</sub>** and **R<sub>18</sub>'** are independently hydrogen or alkyl of one to six carbons; or **R<sub>18</sub>** and **R<sub>18</sub>'** together are a cycloheteroalkyl ring or a cycloalkyl ring of three to eight carbons;

In another embodiment of the invention are disclosed methods of selectively partially

antagonizing, antagonizing, agonizing or modulating the glucocorticoid receptor.

In another embodiment of the invention are disclosed methods of treating diseases

comprising administering an effective amount of a compound having Formula I.

In yet another embodiment of the invention are disclosed pharmaceutical compositions containing compounds of Formula I.

Compounds of this invention include, but are not limited to,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinoline-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-2,2,4,N-tetramethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinolin-10-amine,

methyl 2,5-dihydro-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline-10-carboxylate,

10-ethenyl-2,5-dihydro-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4f]quinoline,

10-ethynyl-2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinolin-10-ol,

10-(difluoromethoxy)-2,5-dihydro-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
10-ethoxy-2,5-dihydro-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinoline-10-ol  
5 acetate (ester),  
5-(3-bromo-5-methylphenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)-  
phenol, acetate (ester),  
10 3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)-  
phenol,  
2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[[3-(methylthio)methoxy]phenyl]-1H-[1]benzopyrano[3,4-f]quinoline,  
[3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)-  
15 phenyl] dimethylcarbamate,  
5-[3-(2-furanyl)-5-methylphenyl]-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[3-methyl-5-(1-morpholinyl)phenyl]-1H-[1]benzopyrano[3,4-f]quinoline,  
20 2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(phenylmethylene)-1H-[1]benzopyrano[3,4-f]quinoline,  
5-(3,5-dichlorophenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
5-butyl-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
25 2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[3-(trifluoromethyl)phenyl]-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(4-methoxyphenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
5-(3-chlorophenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
30 2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(3-methylphenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
(±)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinoline,  
35 (±)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinoline,  
5-(3,5-dimethylphenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

- 5-(4-chlorophenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
5-(3,4-dimethylphenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
5 5-(4-fluorophenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
5-[3,5-bis(trifluoromethyl)phenyl]-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
(-)-5-(3,5-dichlorophenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
10 (+)-5-(3,5-dichlorophenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
5-(3,5-difluorophenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
15 2,5-dihydro-10-methoxy-2,2,4,N-tetramethyl-N-phenyl-1H-[1]benzopyrano[3,4-f]quinolin-5-amine,  
(-)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
(+)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
20 2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
4-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)-N,N-dimethylbenzenamine,  
2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(5-methoxy-2-thienyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
25 2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(5-propyl-2-thienyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[4-(1-morpholinyl)phenyl]-1H-[1]benzopyrano[3,4-f]quinoline,  
30 1-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)-3,3-dimethyl-2-butanone,  
2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline-5-carbonitrile,  
1-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)-2-propanone,  
35 methyl-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline-5-acetate,

2-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)-1-phenylethanone,

5-[2-(chloromethyl)-2-propenyl]-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-(methylene-1H-[1]benzopyrano[3,4-f]quinoline-5-propanol, acetate (ester),

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(4-methylphenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

5-(3-fluoro-4-methylphenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-

[1]benzopyrano[3,4-f]quinoline,

5-(3-bromophenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(phenylmethyl)-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-propyl-1H-[1]benzopyrano[3,4-f]quinoline,

5-(4-fluorophenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

5-(3-fluorophenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-2,2,4,5-tetramethyl-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(1-methylethyl)-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(2-methylpropyl)-1H-[1]benzopyrano[3,4-f]quinoline,

5-ethyl-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline-5-carboximidic acid ethyl ester,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-(methylene 1H-[1]benzopyrano[3,4-f]quinoline-5-propanol,

2,5-dihydro-10-methoxy-2,2,4,N,N-pentamethyl-1H-[1]benzopyrano[3,4-f]quinoline-5-acetamide,

2,5-dihydro-10-methoxy-2,2,4,N,N-pentamethyl-1H-[1]benzopyrano[3,4-f]quinoline-5-ethanamine,

N-cyclopropyl-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline-5-acetamide,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(2-propynyl)-1H-[1]benzopyrano[3,4-f]quinoline,

5-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)-  
2(5H)-furanone,

5-(3-butenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
f]quinoline,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline-5-propanol,

10-ethyl-2,5-dihydro-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-2,2,4,10-tetramethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinoline,

5-(3,5-dichlorophenyl)-10-ethyl-2,5-dihydro-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
f]quinoline,

5-(3,5-dichlorophenyl)-2,5-dihydro-2,2,4,N-tetramethyl-1H-[1]benzopyrano[3,4-  
f]quinolin-10-amine,

5-(3,5-dichlorophenyl)-2,5-dihydro-2,2,4-trimethyl-N-(2-propenyl)-1H-  
[1]benzopyrano[3,4-f]quinolin-10-amine,

2,5-dihydro-2,2,4-trimethyl-5-phenyl-10-(2-propynyloxy)-1H-[1]benzopyrano[3,4-  
f]quinoline,

2,5-dihydro-2,2,4-trimethyl-5-phenyl-10-(2-propenyloxy)-1H-[1]benzopyrano[3,4-  
f]quinoline,

2,5-dihydro-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline-10-  
methanol,

2,5-dihydro-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline-10-  
carboxylic acid,

5-(3,5-dichlorophenyl)-10-ethoxy-2,5-dihydro-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
f]quinoline,

5-(3,5-dichlorophenyl)-2,5-dihydro-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-  
10-ol,

5-(3,5-dichlorophenyl)-2,5-dihydro-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-  
10-yl]methylcarbonate,

2,5-dihydro-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinolin-10-ol,

10-(bromodifluoromethoxy)-2,5-dihydro-2,2,4-trimethyl-5-(2-propenyl)-1H-

[1]benzopyrano[3,4-f]quinoline,

[3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)-  
phenyl] methylcarbonate,

2,5-dihydro-10-methoxy-5-(3-methoxyphenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
f]quinoline,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[3-(2-propenyloxy)phenyl]-1H-  
[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[3-(phenylmethoxy)phenyl]-1H-  
[1]benzopyrano[3,4-f]quinoline,

- 5-[3-(cyclopropylmethoxy)phenyl]-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[3-[2-(1-piperidinyl)ethoxy]phenyl]-1H-[1]benzopyrano[3,4-f]quinoline,  
5 5-(3-hexyloxyphenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
5-[3-(2,4-dinitrophenoxy)phenyl]-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[3-(2-propynyloxy)phenyl]-1H-[1]benzopyrano[3,4-f]quinoline,  
10 3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)phenol, 4-methylbenzenesulfonate (ester),  
4-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)phenolacetate (ester),  
15 4-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)phenol,  
2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[[4-(methylthio)methoxy]phenyl]-1H-[1]benzopyrano[3,4-f]quinoline,  
[4-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)phenyl] dimethylcarbamate,  
20 2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[4-(phenylmethoxy)phenyl]-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[3-(methoxymethoxy)phenyl]-1H-[1]benzopyrano[3,4-f]quinoline,  
25 [(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)phenyl] 1-morpholinecarboxylate,  
2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[3-[(methylsulfinyl)methoxy]phenyl]-1H-[1]benzopyrano[3,4-f]quinoline,  
O-[3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)phenyl] ester,  
30 2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[3-(methylthio)phenyl]-1H-[1]benzopyrano[3,4-f]quinoline,  
O-[3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)phenyl] methylcarbonothioate,  
35 [3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl)-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)phenyl] trifluoromethanesulfonate,  
5-[3-(4,5-dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

ethyl 3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)benzoate,

3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)benzoic acid,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[3-methyl-5-(2-propenyl)phenyl]-1H-[1]benzopyrano[3,4-f]quinoline,

1-[3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)-5-methylphenyl]ethanone,

3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)-5-trimethylbenzenemethanol,

5-[3-(2-furanyl)phenyl]-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[3-methyl-5-(1H-pyrrolidin-1-yl)phenyl]-1H-[1]benzopyrano[3,4-f]quinoline,

3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-methyl)-5,N-dimethylbenzenamine,

3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)-5-methyl-N-(2-propenyl)benzamide,

3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)-N-(2-methoxyethyl)-5-methylbenzenamine,

3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)-N-(2-propenyl)benzenamine,

N'-[3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)-5-methylphenyl]-N,N-dimethylurea,

N-[3-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl)phenyl]benzenemethanamine,

5-[(3,5-dichlorophenyl)methylene]-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

5-[(4-chlorophenyl)methylene]-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[[3-(trifluoromethyl)-phenyl]methylene]-1H-[1]-benzopyrano[3,4-f]quinoline,

5-[(2,6-difluorophenyl)methylene]-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

5-[(2-chlorophenyl)methylene]-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

5-[(2,6-dichlorophenyl)methylene]-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

5-[(2-fluorophenyl)methylene]-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-[(4,5-dihydro-4,4-dimethyl-2-oxazolyl)methylene]-1H-[1]benzopyrano[3,4-f]quinoline,  
5 2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(2-pyridinylmethylene)-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(2-thienyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-9,10-dimethoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
10 5-(2-cyclohexen-1-yl)-2,5-dihydro-9,10-dimethoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(3-methyl-3-butenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
15 2,5-dihydro-10-methoxy-5-(5,5-dimethyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
*rel* (5R,2'R) 2,5-dihydro-10-methoxy-5-(2-oxo-3-tetrahydropyranyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
*anti*(5R, 2'S) 2,5-dihydro-10-methoxy-5-(2-oxo-3-tetrahydropyranyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
20 2,5-dihydro-10-methoxy-5-(3-cyclopentenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
25 2,5-dihydro-10-methoxy-5-(3-butenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(1-ethenyl-1-cyclohexyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(4,4-dimethyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
30 2,5-dihydro-10-methoxy-5-(1-methylene-2-cyclohexyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(1-oxo-2-cyclohexyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
35 2,5-dihydro-10-methoxy-5-(3-cyclooctenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(3-cycloheptenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

- 2,5-dihydro-10-methoxy-5-(1-cyclohexenylmethyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(3,3-dimethyl-6-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
5 2,5-dihydro-10-methoxy-5-(2-bromo-3-propenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
*rel*(5R,3'R) 2,5-dihydro-10-methoxy-5-(1-hydroxymethyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
*rel*(5R,3'S) 2,5-dihydro-10-methoxy-5-(1-hydroxymethyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
10 2,5-dihydro-10-methoxy-5-(3-hydroxymethyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(3-indolyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
15 *rel* (5S,3'S) 2,5-dihydro-10-methoxy-5-(1-methyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
*rel* (5R,3'S) 2,5-dihydro-10-methoxy-5-(1-methyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
(-) (5S,3'S) 2,5-dihydro-10-methoxy-5-(1-methyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
20 (-) (5S,3'R) 2,5-dihydro-10-methoxy-5-(1-hydroxymethyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
(+) (5R,3'S) 2,5-dihydro-10-methoxy-5-(1-hydroxymethyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
25 (-)-(5S,3'R) 2,5-dihydro-10-methoxy-5-(1-methyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
(+)-(5R,3'S) 2,5-dihydro-10-methoxy-5-(1-methyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(1-chloromethyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
30 *rel* (5R,3'R) 2,5-dihydro-10-methoxy-5-(1-methoxymethyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
*rel* (5R,3'R) 2,5-dihydro-10-methoxy-5-(1-methylthiomethyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
35 *rel* (5R,3'S) 2,5-dihydro-10-methoxy-5-(1-acetoxymethyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
*rel* (5R,3'R) 2,5-dihydro-10-methoxy-5-(1-acetoxymethyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

*rel* (5R, 3'R) 2,5-dihydro-10-methoxy-5-(1-methoxymethyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
*rel* (5R, 3'R) 2,5-dihydro-10-methoxy-5-(1-(N,N-dimethylamino)methyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
5 *rel* (5R, 3'S) 2,5-dihydro-10-methoxy-5-(1-methylthiomethyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
*rel* (5R, 3'R) 2,5-dihydro-10-methoxy-5-(1-(N-morpholino)methyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
*rel* (5R, 3'R) 2,5-dihydro-10-methoxy-5-(1-(N-methyl-N-methylsulfonylamino)methyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
10 *rel* (5R, 3'S) 2,5-dihydro-10-methoxy-5-(1-(N,N dimethylamino)methyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
*rel* (5R, 3'R) 2,5-dihydro-10-methoxy-5-(1-(N-methylamino)methyl-3-cyclohexenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
15 2,5-dihydro-10-methoxy-5-(2-methyl-3-propenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(1,3-butadien-2-yl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(2-carbomethoxy-3-propenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
20 [1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(1,2-dihydroxy-3-propyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(1,2-epoxy-3-propenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
25 2,5-dihydro-10-methoxy-5-(1-(N-phthalimido)-3-propyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(1-amino-3-propyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(1-(hydrazinocarbonylamino)-3-propyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
30 (E) 2,5-dihydro-10-methoxy-5-(2-carbomethoxy-1-ethenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
(Z)-2,5-dihydro-10-methoxy-5-(1-propenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
35 (E) 2,5-dihydro-10-methoxy-5-(3-hydroxy-1-propenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
(E) 2,5-dihydro-10-methoxy-5-(3-(N,N-dimethylaminocarbonyloxy)-1-propenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

(E) 2,5-dihydro-10-methoxy-5-(3-methoxymethoxy-1-propenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-5-(3-hydroxy-3-propenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

5 methyl 2-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl) acetyl hydroxamate,

2-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl) acetaldehyde,

2,5-dihydro-10-methoxy-5-(2-cyclohexylidenylethyl)-2,2,4-trimethyl-1H-

10 [1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-5-(2-cyclopentylidenylethyl)-2,2,4-trimethyl-1H-

[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-5-(2-cycloheptylidenylethyl)-2,2,4-trimethyl-1H-

[1]benzopyrano[3,4-f]quinoline,

15 2,5-dihydro-10-methoxy-5-(3-methyl-2-butenyl)-2,2,4-trimethyl-1H-

[1]benzopyrano[3,4-f]quinoline,

trans 2,5-dihydro-10-methoxy-5-(2-butenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

trans 2,5-dihydro-10-methoxy-5-(2-penten-1-yl)-2,2,4-trimethyl-1H-

20 [1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-5-(1,1-difluoro-1-propen-3-yl)-2,2,4-trimethyl-1H-

[1]benzopyrano[3,4-f]quinoline,

(E) methyl 2-(2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinolin-5-yl) 2-butenate,

25 (E) 2,5-dihydro-10-methoxy-5-(4-hydroxy-2-buten-1-yl)-2,2,4-trimethyl-1H-

[1]benzopyrano[3,4-f]quinoline,

(E) 2,5-dihydro-10-methoxy-5-(4-(N,N-dimethylaminocarbonyloxy)-2-buten-1-yl)-

2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

(E) 2,5-dihydro-10-methoxy-5-(4-(N-methylaminocarbonyloxy)-2-buten-1-yl)-2,2,4-

30 trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

(E) 2,5-dihydro-10-methoxy-5-(2-butenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-5-(2-hydroxyethyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

35 2,5-dihydro-10-methoxy-5-(2-(N-benzylcarbonyloxy)ethyl)-2,2,4-trimethyl-1H-

[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-5-(2-(N-morpholinocarbonyloxy)ethyl)-2,2,4-trimethyl-1H-

[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-5-(2-(N-(2-methoxyethyl)aminocarbonyloxy)ethyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(2-(N-methyaminocarbonyloxyoxy)ethyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
5 2,5-dihydro-10-methoxy-5-(2-(N,N-dimethylaminocarbonyloxy)ethyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(2-methoxymethoxyethyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(2,2-dimethylethoxycarbonylamino)methyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
10 2,5-dihydro-10-methoxy-5-(aminomethyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(ethoxycarbonylamino)methyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
15 2,5-dihydro-10-methoxy-5-(carboethoxy)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(cyclopentyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(1-methylpropa-1,2-dienyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
20 2,5-dihydro-10-methoxy-5-(3,4,5-trifluorophenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(cyclohexyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
25 2,5-dihydro-10-methoxy-5-(2-pyridyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(3-pyridyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(4-pyridyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
30 (10-chloro-9-hydroxy-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,  
10-chloro-9-hydroxy-5-phenyl-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
35 10-chloro-9-hydroxy-5-(3-trifluoromethylphenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
10-chloro-9-hydroxy-5-(3,5-dimethylphenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,

*rel*-(5*S*, 3'*R*)-9-hydroxy-10-methoxy-5-[1-hydroxymethyl-3-cyclohexenyl]-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-*f*]quinoline,  
(-) 2,5(*S*)-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-(3*S*-cyclopentenyl)-1H-[1]benzopyrano[3,4-*f*]quinoline,  
5 (-) 2,5(*S*)-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-(3*R*-cyclopentenyl)-1H-[1]benzopyrano[3,4-*f*]quinoline,  
10-chloro-9-hydroxy-5-(3,5-dichlorophenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-*f*]quinoline,  
(+)-(5*R*, 3'*S*) 2,5-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-(3-cyclopentenyl)-1H-[1]benzopyrano[3,4-*f*]quinoline,  
10 (+)-(5*R*, 3'*R*) 2,5-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-(3-cyclopentenyl)-1H-[1]benzopyrano[3,4-*f*]quinoline,  
10-chloro-9-hydroxy-5-(3,4-difluorophenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-*f*]quinoline,  
15 9-10-methylenedioxy-5-phenyl-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-*f*]quinoline,  
5-(3-propenyl)-9-chloro-10-ethenyl-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-*f*]quinoline,  
9-chloro-10-methoxy-5-phenyl-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-*f*]quinoline,  
20 5-(3-propenyl)-9-chloro-10-difluoromethoxy-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-*f*]quinoline,  
9-chloro-10-difluoromethoxy-5-phenyl-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-*f*]quinoline,  
25 8-fluoro-10-methoxy-5-phenyl-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-*f*]quinoline,  
5-(3-propenyl)-8-fluoro-10-methoxy-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-*f*]quinoline,  
(10-methoxy-9-fluoro-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-*f*]quinoline,  
30 10-methoxy-9-hydroxy-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-*f*]quinoline,  
(+/-) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-cyclohexenyl)-1H-[1]benzopyrano[3,4-*f*]quinoline,  
35 (+/-) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(1-methylcyclohexen-3-yl)-1H-[1]benzopyrano[3,4-*f*]quinoline,  
(-) (5*S*, 3'*S*)-9-hydroxy-5-[1-methyl-3-cyclohexenyl]-10-methoxy-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-*f*]quinoline,

(+) (5R,3'R)-9-hydroxy-5-[1-methyl-3-cyclohexenyl]-10-methoxy-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,

(+) (5R,3'S)-9-hydroxy-5-[1-methyl-3-cyclohexenyl]-10-methoxy-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,

(-) (5S,3'R)-9-hydroxy-5-[1-methyl-3-cyclohexenyl]-10-methoxy-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,

*rel*-(5S,3'R)-9-hydroxy-5-[1-hydroxymethyl-3-cyclohexenyl]-10-methoxy-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,

(+/-) (5S,3'R) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(1-methylcyclohexen-3-yl)-1H-[1]benzopyrano[3,4-f]quinoline,

*rel*-(5S,3'R)-9-hydroxy-5-[1-methoxymethyl-3-cyclohexenyl]-10-methoxy-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-9-hydroxy-10-methoxy-5-propyl-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

(-) (5S,3'S) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-cycloheptenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

(-) (5S,3'R) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-cycloheptenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3,5-difluorophenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3,4,5-trifluorophenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

5-butyl-2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

(-) (5S,3'S) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-cyclopentenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

(-) (5S,3'R) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-cyclopentenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3,4-difluorophenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(4-fluorophenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-trifluoromethylphenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3,5-bis(trifluoromethyl)phenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

- 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-trifluoromethyl-4-chlorophenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(2-methylpropyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 5 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-fluoro-4-chlorophenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-butenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-methoxy-5-(phenylmethyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
 10 (-) (5S,3'R) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-[1-ethyl-3-cyclohexenyl]-1H-[1]benzopyrano[3,4-f]quinoline,  
 (-) (S) 5-cyclopentyl-2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
 15 (+) (R) 5-cyclopentyl-2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-methoxy-5-(3-propynyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(2-propyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 20 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(5-methoxy-2-thienyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 (±) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(2,3,4,5,6-pentafluorophenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 25 (+/-) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5(S)-(3(S)-1-hydroxymethylcyclopenten-3-yl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 (+/-) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5(S)-(3(S)-1-methylcarboxylatecyclopenten-3-yl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 (-) (5S,3'S) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-cyclohexenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 30 (-) (5S,3'R) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-cyclohexenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(2-thienyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 35 (±) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(2-methylphenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(2-acetoxymethyl-3-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

(+) (5R,3'S) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-[1-ethyl-3-cyclohexenyl]-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-cyclohexyl-1H-[1]benzopyrano[3,4-f]quinoline,  
 5 2,5,5-trihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(2-hydroxymethyl-3-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 methyl 2-[2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]-5-quinolinyl] acetate,  
 10 (Z) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(2-butenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-methyl-2-butenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 15 (+) (5S,3'S) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-cyclohexenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 (+) (5R,3'R) 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-cyclohexenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 (+) (5R,3'S) 2,5(R)-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-cyclopentenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 20 (+) (5R,3'R) 2,5(R)-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-cyclopentenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 rel-(5S)-9-hydroxy-5-[(3R)-(1-methoxycarbonyl)cyclohexen-3-yl]-10-methoxy-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,  
 25 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(2-methyl-3-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 9,10-Dimethoxy-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
 9,10-Dimethoxy-5-[3-cyclohexenyl]-methoxy-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,  
 30 10-methoxy-9-ethoxy-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
 10-methoxy-9-(3-propenyloxy)-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
 35 10-methoxy-9-(3-propenyloxy)-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-acetoxy-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

- 2,5-dihydro-9-(4-N,N-dimethylamino-4-oxo-butanoyloxy)-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
7-bromo-5-[3-cyclohexenyl]-10-methoxy-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,  
5 10-methoxy-7-bromo-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
7-bromo-5-[1-methyl-3-cyclohexenyl]-10-methoxy-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,  
10-methoxy-9-bromo-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-  
10 [1]benzopyrano[3,4-f]quinoline,  
7,9-Dibromo-10-methoxy-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
7,9-Dibromo-5-[cyclohexen-3-yl]-10-methoxy-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,  
15 7,9-Dibromo-5-[1-methyl-3-cyclohexenyl]-10-methoxy-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,  
10-methoxy-7-(2-ethenyl)-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
10-methoxy-7-methyl-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-  
20 [1]benzopyrano[3,4-f]quinoline,  
10-methoxy-7-acetyl-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
(+/-) 2,5-dihydro-9-methyl-10-methoxy-2,2,4-trimethyl-5-(1-methylcyclohexen-3-yl)-1H-[1]benzopyrano[3,4-f]quinoline,  
25 10-methoxy-7-methyl-9-methyl-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
10-chloro-5-(3-propenyl)-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,  
(+/-) 2,5-dihydro-10-chloro-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinoline,  
30 2,5-dihydro-10-methoxy-5-(3-(N-methyl-N-(carbomethoxymethyl)aminocarbonyloxy)phenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(3-(N-methyl-N-(N-methylcarbonyl)aminocarbonyloxy)phenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
35 2,5-dihydro-10-methoxy-5-(3-(N-methylaminocarbonyloxy)phenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-methoxy-5-(3-(2-hydroxyethyl)phenyl)-2,2,4-trimethyl-1H-  
[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(3-(2-methanesulfonyloxyethyl)phenyl)-2,2,4-trimethyl-1H-  
[1]benzopyrano[3,4-f]quinoline,  
5 2,5-dihydro-10-methoxy-5-(3-(2-methylthioethyl)phenyl)-2,2,4-trimethyl-1H-  
[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(3-(2-(N,N-dimethylaminocarbonyloxy)ethyl)phenyl)-2,2,4-  
trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(3-(2-(N,N-dimethylamino)ethyl)phenyl)-2,2,4-trimethyl-1H-  
10 [1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-cyclopropyl-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
f]quinoline,  
2,5-dihydro-10-methoxy-5-ethenyl-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
trans 2,5-dihydro-10-methoxy-5-(2-phenylethenyl)-2,2,4-trimethyl-1H-  
15 [1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-5-(2-phenylethynyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
f]quinoline,  
cis 2,5-dihydro-10-methoxy-5-(2-phenylethenyl)-2,2,4-trimethyl-1H-  
[1]benzopyrano[3,4-f]quinoline,  
20 2,5-dihydro-10-methoxy-5-(2-methylpropenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
f]quinoline,  
trans 2,5-dihydro-10-methoxy-5-(1-cyclohexenyl)-2,2,4-trimethyl-1H-  
[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-(2-furanyl)-5-(3-propenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
25 f]quinoline,  
2,5-dihydro-10-cyano-5-(3-propenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
f]quinoline,  
2,5-dihydro-10-carboxy-5-(3-propenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
f]quinoline,  
30 2,5-dihydro-10-(2-hydroxymethyl)-5-(3-propenyl)-2,2,4-trimethyl-1H-  
[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-formyl-5-(3-propenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
f]quinoline,  
2,5-dihydro-10-aminomethyl-5-(3-propenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
35 f]quinoline,  
2,5-dihydro-10-methoxymethyl-5-(3-propenyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
f]quinoline,  
2,5-dihydro-10-ethenyl-5-phenyl-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-10-ethynyl-5-phenyl-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
methyl 2,5-dihydro-5-phenyl-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline-10-  
carboxylate,  
2,5-dihydro-10-(hydroxymethyl)-5-phenyl-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
5 f]quinoline,  
2,5-dihydro-10-formyl-5-phenyl-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-(methoxymethyl)-5-phenyl-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
f]quinoline,  
2,5-dihydro-10-ethenyl-5-oxo-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
10 5-(3-cyclohexenyl)-2,5-dihydro-10-ethenyl-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
f]quinoline,  
2,5-dihydro-10-ethenyl-5-[1-methyl-3-cyclohexenyl]-2,2,4-trimethyl-1H-  
[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-5-(3-propenyl)-10-methylthio-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
15 f]quinoline,  
2,5-dihydro-5-(3-propenyl)-10-methylthio-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
f]quinoline,  
(+/-) 2,5-dihydro-9-(4-acetamidobutanoyloxy)-10-methoxy-2,2,4-trimethyl-5-allyl-1H-  
[1]benzopyrano[3,4-f]quinoline,  
20 10-(difluoromethoxy)-2,5-dihydro-5-phenyl-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-  
f]quinoline,  
10-(bromodifluoromethoxy)-2,5-dihydro-5-phenyl-2,2,4-trimethyl-1H-  
[1]benzopyrano[3,4-f]quinoline,  
10-(bromodifluoromethoxy)-5-phenyl-2,2-dimethyl-4-methylene-2,3,4,5-tetrahydro-1H-  
25 chromeno[3,4-f]quinoline,  
2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-((2-fluorophenyl)methyl)-1H-  
[1]benzopyrano[3,4-f]quinoline,  
10-methoxy-5-(5-methylisoxazol-3-yl)methyidene-2,5-dihydro-5-phenyl-2,2,4-  
trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
30 10-methoxy-5-(3-methylisoxazol-5-yl)methyidene-2,5-dihydro-5-phenyl-2,2,4-  
trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
10-methoxy-5-(4,5-dimethyl-1,3-oxazol-2-yl)methyidene-2,5-dihydro-5-phenyl-2,2,4-  
trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
10-methoxy-5-(6-chloropyridin-2-yl)methyidene-2,5-dihydro-5-phenyl-2,2,4-trimethyl-  
35 1H-[1]benzopyrano[3,4-f]quinoline,  
10-methoxy-5-(pyridin-2-yl)methyidene-2,5-dihydro-5-phenyl-2,2,4-trimethyl-1H-  
[1]benzopyrano[3,4-f]quinoline,

10-methoxy-5-(but-3-enylidene)-2,5-dihydro-5-phenyl-2,2,4-trimethyl-1H-  
[1]benzopyrano[3,4-f]quinoline,  
10-methoxy-5-(1-methylpropylidene)-2,5-dihydro-5-phenyl-2,2,4-trimethyl-1H-  
[1]benzopyrano[3,4-f]quinoline,  
5 10-methoxy-5-(1-butylidene)-2,5-dihydro-5-phenyl-2,2,4-trimethyl-1H-  
[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-2,2,4-trimethyl-3-oxide-5-phenyl-1H-[1]benzopyrano[3,4-  
f]quinazoline,  
2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-  
10 f]quinazoline,  
2,5-dihydro-10-methoxy-2,2-[spiro(tetrahydro-4-pyranyl)]-4-methyl-5-allyl-1H-  
[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-2,2-[spiro(hexyl)]-5-allyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-2,2-diethyl-4-methyl-5-allyl-1H-[1]benzopyrano[3,4-  
15 f]quinoline,  
2,5-dihydro-10-methoxy-2,2,3,4-tetramethyl-5-allyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-10-methoxy-2,2-dimethyl-4-ethyl-5-allyl-1H-[1]benzopyrano[3,4-  
f]quinoline,  
2,5-dihydro-10-methoxy-2,2,3-trimethyl-5-allyl-1H-[1]benzopyrano[3,4-f]quinoline,  
20 Z-5-(benzylidenyl)-9-hydroxy-10-methoxy-2,2,4-trimethyl-1H-2,5-dihydro-  
[1]benzopyrano[3,4-f]quinoline,  
Z-5-(2,5-difluorobenzylidenyl)-9-hydroxy-10-methoxy-2,2,4-trimethyl-1H-2,5-dihydro-  
[1]benzopyrano[3,4-f]quinoline,  
Z-5-(3-fluorobenzylidenyl)-10-chloro-9-hydroxy-2,2,4-trimethyl-2,5-dihydro-1H-  
25 [1]benzopyrano[3,4-f]quinoline,  
Z-10-chloro-9-hydroxy-5-(2-picolinylidenyl)-2,2,4-trimethyl-2,5-dihydro-1H-  
[1]benzopyrano[3,4-f]quinoline,  
Z-9-hydroxy-10-methoxy-5-(2-picolinylidenyl)-2,2,4-trimethyl-2,5-dihydro-1H-  
[1]benzopyrano[3,4-f]quinoline,  
30 9-hydroxy-10-methoxy-5-(3,5-difluorophenyl)methylidene-2,5-dihydro-5-phenyl-2,2,4-  
trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
9-hydroxy-10-methoxy-5-(3,4-difluorophenyl)methylidene-2,5-dihydro-5-phenyl-2,2,4-  
trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
(Z) 9-hydroxy-10-methoxy-5-((4-fluorophenyl)methylene)-2,2,4-trimethyl-1H-2,5-  
35 dihydro-[1]benzopyrano[3,4-f]quinoline,  
(Z)-9-hydroxy-10-methoxy-5-([2,3-difluorophenyl]methylene)-2,2,4-trimethyl-1H-2,5-  
dihydro-[1]benzopyrano[3,4-f]quinoline,

- Z-5-(3-fluorobenzylidenyl)-10-methoxy-9-hydroxy-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,  
*rel*-(5S,3'R)-9-hydroxy-5-[1-methoxymethyl-3-cyclohexenyl]-10-chloro-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,  
 5 9-hydroxy-10-methoxy-5-ethyl-2,2,4-trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,  
 (+/-) 2,5-dihydro-9-cyanomethoxy-10-methoxy-2,2,4-trimethyl-5-allyl-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-(4-N,N-diethylamino-4-oxo-butanoyloxy)-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 10 2,5-dihydro-9-(4-N-piperidino-4-oxo-butanoyloxy)-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-(4-N-morpholino-4-oxo-butanoyloxy)-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 15 2,5-dihydro-9-(4-N,N-dimethylamino-4-oxo-butanoyloxy)-10-methoxy-2,2,4-trimethyl-5-(3,4,5-trifluorophenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-5-difluorophenylmethyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-(2-thienyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 20 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-cyclopentyl-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-((2-fluorophenyl)methyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 25 2,5-dihydro-9-hydroxymethyl-10-methoxy-2,2,4-trimethyl-5-allyl-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(1-pentenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-methylcarboxylate-10-methoxy-2,2,4-trimethyl-5-allyl-1H-[1]benzopyrano[3,4-f]quinoline,  
 30 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-allenyl-1H-[1]benzopyrano[3,4-f]quinoline,  
 (-) (5S, 3'S) 2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(cyclopenten-3-yl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 35 (-) (5S, 3'S) 2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(cyclohexen-3-yl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 (-) (5S, 3'R) 2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(cyclohexen-3-yl)-1H-[1]benzopyrano[3,4-f]quinoline,

(-) (5S, 3'R) 2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(cyclopenten-3-yl)-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3(Z)-pentenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
5 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-acetoxyphenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
10-difluoromethoxy-5-[[3-(methylthio)methoxy]phenyl]-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-7-bromo-9-hydroxy-10-chloro-2,2,4-trimethyl-5-allyl-1H-[1]benzopyrano[3,4-f]quinoline,  
10 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-hydroxyphenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-9-methylthiomethoxy-10-methoxy-2,2,4-trimethyl-5-(3-(methylthio)methoxyphenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
15 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-(methylthiomethoxy)phenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
9-hydroxy-10-chloro-5-(phenylmethylene)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-((2-N,N-dimethylcarbamoyloxy)phenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
20 2,5-dihydro-9-N,N-dimethylcarbamoyloxy-10-methoxy-2,2,4-trimethyl-5-((2-N,N-dimethylcarbamoyloxy)phenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-ethyl-1H-[1]benzopyrano[3,4-f]quinoline,  
25 2,5-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-isopropyl-1H-[1]benzopyrano[3,4-f]quinoline,  
9-hydroxy-10-methoxy-5-(phenylmethylene)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-butyl-1H-[1]benzopyrano[3,4-f]quinoline,  
30 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(1-thiazol-2-yl)-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-(2-methylpropyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
35 2,5-dihydro-9-hydroxymethyl-10-chloro-2,2,4-trimethyl-5-allyl-1H-[1]benzopyrano[3,4-f]quinoline,  
2,5-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-propyl-1H-[1]benzopyrano[3,4-f]quinoline,

9-hydroxy-10-methoxy-5-([3-fluorophenyl]methylene)-2,2,4-trimethyl-1H-2,5-dihydro-  
[1]benzopyrano[3,4-f]quinoline,

9-hydroxy-10-chloro-5-([2-pyridyl]methylene)-2,2,4-trimethyl-1H-2,5-dihydro-  
[1]benzopyrano[3,4-f]quinoline,

5 rel-(5S)-9-hydroxy-5-[(3S)-(1-hydroxymethyl)cyclohexen-3-yl]-10-methoxy-2,2,4-  
trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,

rel-(5S)-9-hydroxy-5-[(3S)-(1-methoxycarbonyl)cyclohexen-3-yl]-10-methoxy-2,2,4-  
trimethyl-2,5-dihydro-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3,5-dichlorophenyl)-1H-  
10 [1]benzopyrano[3,4-f]quinoline,

(-) (5S,3'S) 2,5-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-(1-methylcyclohexen-3-  
yl)-1H-[1]benzopyrano[3,4-f]quinoline,

(-) (5S,3'R) 2,5-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-(1-methylcyclohexen-3-  
yl)-1H-[1]benzopyrano[3,4-f]quinoline,

15 (+) (5R,3'S) 2,5-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-(1-methylcyclohexen-3-  
yl)-1H-[1]benzopyrano[3,4-f]quinoline,

(+) (5R,3'R) 2,5-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-(1-methylcyclohexen-  
3-yl)-1H-[1]benzopyrano[3,4-f]quinoline,

(+/-) 2,5-dihydro-9-(4-N,N-dimethylamino-4-oxo-butanoyloxy)-10-chloro-2,2,4-  
20 trimethyl-5-allyl-1H-[1]benzopyrano[3,4-f]quinoline,

(-) 2,5-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-cyclopentyl-1H-  
[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-9-(4-N,N-dimethylamino-4-oxo-butanoyloxy)-10-methoxy-2,2,4-trimethyl-  
5-(1-methylethyl)-1H-[1]benzopyrano[3,4-f]quinoline,

25 2,5-dihydro-9-(4-N,N-dimethylamino-4-oxo-butanoyloxy)-10-methoxy-5-  
(phenylmethyl)-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-9-(4-N,N-dimethylamino-4-oxo-butanoyloxy)-10-methoxy-2,2,4-trimethyl-  
5-(2-thienyl)-1H-[1]benzopyrano[3,4-f]quinoline,

2,5-dihydro-9-(4-N,N-dimethylaminobutanoyloxy)-10-methoxy-2,2,4-trimethyl-5-(2-  
30 propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,

9-(2-ethoxy-2-oxo-ethylaminocarbonyl)-oxy-10-methoxy-5-(3-propenyl)-2,2,4-  
trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,

(+/-) 2,5-dihydro-9-(3-acetamido-propanoyloxy)-10-methoxy-2,2,4-trimethyl-5-allyl-1H-  
[1]benzopyrano[3,4-f]quinoline,

35 (+/-) 2,5-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-benzyl-1H-  
[1]benzopyrano[3,4-f]quinoline,

9-hydroxy-10-methoxy-5-(phenylmethylene)-2,2,4-trimethyl-1H-2,5-dihydro-  
[1]benzopyrano[3,4-f]quinoline,

9-(dimethylaminothiocarbonyl)-oxy-10-methoxy-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
 (+/-) 2,5-dihydro-9-(N-carbamoyl-2-aminoacetoxyl)-10-methoxy-2,2,4-trimethyl-5-allyl-1H-[1]benzopyrano[3,4-f]quinoline,  
 (+/-) 2,5-dihydro-9-(4-ethoxy-4-oxo-butoxy)-10-methoxy-2,2,4-trimethyl-5-allyl-1H-[1]benzopyrano[3,4-f]quinoline,  
 (+/-) 2,5-dihydro-9-(4-oxo-pentanoyloxy)-10-methoxy-2,2,4-trimethyl-5-allyl-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-chloro-2,2,4-trimethyl-5-(3,4,5-trifluorophenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-methylthiomethoxy-10-methoxy-2,2,4-trimethyl-5-allyl-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-(4-N,N-diethylamino-4-oxo-pentanoyloxy)-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-(4-N,N-dimethylamino-4-oxo-pentanoyloxy)-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-(4-N-piperidino-4-oxo-pentanoyloxy)-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-(4-N-morpholino-4-oxo-pentanoyloxy)-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 (-) 2,5-dihydro-9-(4-N,N-dimethylamino-4-oxo-butanoyloxy)-10-methoxy-2,2,4-trimethyl-5(S)-(3(S)-1-cyclopenten-3-yl)-1H-[1]benzopyrano[3,4-f]quinoline,  
 10-methoxy-9-(allylaminocarbonyl)oxy-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
 10-methoxy-9-(cyclohexylaminocarbonyl)-oxy-5-(3-propenyl)-2,2,4-trimethyl-1H-2,5-dihydro-[1]benzopyrano[3,4-f]quinoline,  
 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(3-thienyl)-1H-[1]benzopyrano[3,4-f]quinoline, and  
 2,5-dihydro-9-hydroxy-10-methoxy-2,2,4-trimethyl-5-(4-(fluorophenyl)methyl)-1H-[1]benzopyrano[3,4-f]quinoline.

### Detailed Description of The Invention

#### Definition of Terms

The term "alkanoyl" refers to an alkyl group attached to the parent molecular group through a carbonyl group.

The term "alkanoyloxy" refers to an alkanoyl group attached to the parent molecular group through an oxygen atom.

The term "alkenyl" refers to a monovalent straight or branched chain group of two to twelve carbons derived from a hydrocarbon having at least one carbon-carbon double bond.

The term "alkoxy" refers to an alkyl group attached to the parent molecular group through an oxygen atom.

The term "alkoxycarbonyl" refers to an ester group, i.e. an alkoxy group attached to the parent molecular moiety through a carbonyl group.

The term "alkyl" refers to a monovalent straight or branched chain group of one to twelve carbons derived from a saturated hydrocarbon.

The term "alkylene" refers to a divalent straight or branched chain group of one to twelve carbons derived from an alkane.

The term "alkynyl" refers to a monovalent straight or branched chain hydrocarbon of two to twelve carbons with at least one carbon-carbon triple bond.

The term "alkynylene" refers to a divalent straight or branched chain group of two to twelve carbons derived from an alkyne.

The term "amino" refers to  $-NH_2$ .

The term "aryl" refers to a mono- or bicyclic carbocyclic ring system having one or two aromatic rings. The aryl group can also be fused to a cyclohexane, cyclohexene, cyclopentane or cyclopentene ring.

The term "carboxy" refers to  $-CO_2H$ .

The term "cycloalkenyl" refers to a monovalent group derived from a cyclic or bicyclic hydrocarbon of three to twelve carbons that has at least one carbon-carbon double bond.

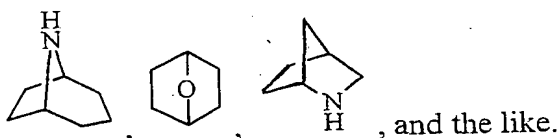
The term "cycloalkyl" refers to a monovalent group three to twelve carbons derived from a saturated cyclic or bicyclic hydrocarbon.

The term "halo" refers to F, Cl, Br, or I.

The term "heterocycle" represents a represents a 4-, 5-, 6- or 7-membered ring containing one, two or three heteroatoms independently selected from the group consisting of nitrogen, oxygen and sulfur. The 4- and 5-membered rings have zero to two double bonds and the 6- and 7-membered rings have zero to three double bonds. The term "heterocycle" also includes bicyclic, tricyclic and tetracyclic groups in which any of the above heterocyclic rings is fused to one or two rings independently selected from an aryl ring, a cyclohexane ring, a cyclohexene ring, a cyclopentane ring, a cyclopentene ring or another monocyclic heterocyclic ring. Heterocycles include acridinyl, benzimidazolyl, benzofuryl, benzothiazolyl, benzothienyl, benzoxazolyl, biotinyl, cinnolinyl, dihydrofuryl, dihydroindolyl, dihydropyranyl, dihydrothienyl, dithiazolyl, furyl, homopiperidinyl, imidazolidinyl, imidazolyl, indolyl, isoquinolyl, isothiazolidinyl, isothiazolyl, isoxazolidinyl, isoxazolyl, morpholinyl,

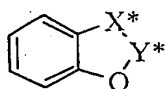
oxadiazolyl, oxazolidinyl, oxazolyl, piperazinyl, piperidinyl, pyranyl, pyrazolidinyl, pyrazinyl, pyrazolyl, pyrazolinyl, pyridazinyl, pyridyl, pyrimidinyl, pyrimidyl, pyrrolidinyl, pyrrolinyl, pyrrolyl, quinolinyl, quinoxaloyl, tetrahydrofuryl, tetrahydroisoquinolyl, tetrahydroquinolyl, tetrazolyl, thiadiazolyl, thiazolidinyl, thiazolyl, thienyl, thiomorpholinyl, triazolyl, and the like.

Heterocyclics also include bridged bicyclic groups where a monocyclic heterocyclic group is bridged by an alkylene group such as



, and the like.

Heterocyclics also include compounds of the formula



where  $X^*$  is selected from  $-CH_2-$ ,  $-CH_2O-$  and  $-O-$ , and  $Y^*$  is selected from  $-C(O)-$  and  $-(C(R''))_v-$ , where  $R''$  is hydrogen or alkyl of one to four carbons, and  $v$  is 1-3. These heterocycles include 1,3-benzodioxolyl, 1,4-benzodioxanyl, and the like.

The term "heterocycloalkyl" as used herein, refers to a non-aromatic, partially unsaturated or fully saturated 4- to 8-membered ring having from one or two heteroatoms independently selected from oxygen, sulfur and nitrogen, in which the nitrogen and sulfur heteroatoms can optionally be oxidized and the nitrogen heteroatom can optionally be quaternized.

The term "N-protected amino" refers to groups intended to protect an amino group against undesirable reactions during synthetic procedures. Commonly used N-protecting groups are disclosed in Greene, "Protective Groups In Organic Synthesis," (John Wiley & Sons, New York (1981)). Preferred N-protecting groups are formyl, acetyl, benzoyl, pivaloyl, t-butylacetyl, phenylsulfonyl, benzyl, t-butyloxycarbonyl (Boc), and benzyloxycarbonyl (Cbz).

The term "O-protected carboxy" refers to a carboxylic acid protecting ester or amide group typically employed to block or protect the carboxylic acid functionality while the reactions involving other functional sites of the compound are performed. Carboxy protecting groups are disclosed in Greene, "Protective Groups in Organic Synthesis" (1981). Additionally, a carboxy protecting group can be used as a prodrug whereby the carboxy protecting group can be readily cleaved in vivo, for example by enzymatic hydrolysis, to release the biologically active parent. Such carboxy protecting groups are well known to those skilled in the art, having been extensively used in the protection of carboxyl groups in the penicillin and cephalosporin fields as described in U.S. Pat. No. 3,840,556 and 3,719,667.

The term "oxo" refers to (=O).

The term "pharmaceutically acceptable prodrugs" represents those prodrugs of the compounds of the present invention which are, within the scope of sound medical judgement, suitable for use in contact with the tissues of humans and lower animals with undue toxicity, irritation, allergic response, and the like, commensurate with a reasonable benefit/risk ratio, and effective for their intended use, as well as the zwitterionic forms, where possible, of the compounds of the invention.

The term "prodrug" represents compounds which are rapidly transformed in vivo to the parent compound of the above formula, for example, by hydrolysis in blood. A thorough discussion is provided in T. Higuchi and V. Stella, Pro-drugs as Novel Delivery Systems, Vol. 14 of the A.C.S. Symposium Series, and in Edward B. Roche, ed., Bioreversible Carriers in Drug Design, American Pharmaceutical Association and Pergamon Press, 1987, both of which are incorporated herein by reference.

The term "pharmaceutically acceptable salt" represents those salts which are, within the scope of sound medical judgement, suitable for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response and the like, and are commensurate with a reasonable benefit/risk ratio. Pharmaceutically acceptable salts are well known in the art. For example, S. M. Berge, *et al.* describe pharmaceutically acceptable salts in detail in *J. Pharmaceutical Sciences*, 1977, 66:1 - 19. The salts can be prepared *in situ* during the final isolation and purification of the compounds of the invention, or separately by reacting the free base function with a suitable organic acid. Representative acid addition salts include acetate, adipate, alginate, ascorbate, aspartate, benzenesulfonate, benzoate, bisulfate, borate, butyrate, camphorate, camphersulfonate, citrate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, fumarate, glucoheptonate, glycerophosphate, hemisulfate, heptonate, hexanoate, hydrobromide, hydrochloride, hydroiodide, 2-hydroxy-ethanesulfonate, lactobionate, lactate, laurate, lauryl sulfate, malate, maleate, malonate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, nitrate, oleate, oxalate, palmitate, pamoate, pectinate, persulfate, 3-phenylpropionate, phosphate, picrate, pivalate, propionate, stearate, succinate, sulfate, tartrate, thiocyanate, toluenesulfonate, undecanoate, valerate salts, and the like. Representative alkali or alkaline earth metal salts include sodium, lithium, potassium, calcium, magnesium, and the like, as well as nontoxic ammonium, quaternary ammonium, and amine cations, including, but not limited to ammonium, tetramethylammonium, tetraethylammonium, methylamine, dimethylamine, trimethylamine, triethylamine, ethylamine, and the like.

Compounds of the present invention can exist as stereoisomers where asymmetric or chiral centers are present. These compounds are designated by the symbols "R" or "S," depending on the configuration of substituents around the chiral carbon atom. The

present invention contemplates various stereoisomers and mixtures thereof. Stereoisomers include enantiomers and diastereomers, and equal mixtures of enantiomers are designated  $(\pm)$ . Individual stereoisomers of compounds of the present invention can be prepared synthetically from commercially available starting materials which contain asymmetric or chiral centers or by preparation of racemic mixtures followed by resolution well-known to those of ordinary skill in the art. These methods of resolution are exemplified by (1) attachment of a mixture of enantiomers to a chiral auxiliary, separation of the resulting mixture of diastereomers by recrystallization or chromatography and liberation of the optically pure product from the auxiliary or (2) direct separation of the mixture of enantiomers on chiral chromatographic columns.

Geometric isomers can also exist in the compounds of the present invention. The present invention contemplates the various geometric isomers and mixtures thereof resulting from the arrangement of substituents around a carbon-carbon double bond or arrangement of substituents around a ring. Substituents around a carbon-carbon double bond are designated as being in the Z or E configuration where the term "Z" represents substituents on the same side of the carbon-carbon double bond and the term "E" represents substituents on opposite sides of the carbon-carbon double bond. The arrangement of substituents around a ring are designated as cis or trans where the term "cis" represents substituents on the same side of the plane of the ring and the term "trans" represents substituents on opposite sides of the plane of the ring. Mixtures of compounds where the substituents are disposed on both the same and opposite sides of plane of the ring are designated cis/trans.

#### Methods for Radioligand Binding Studies with Human Glucocorticoid and Progesterone Receptor Cytosol

The procedure described in Anal. Biochem. 1970, 37, 244-252, hereby incorporated by reference, was used. Briefly, cytosol preparations of human glucocorticoid receptor- $\alpha$  GRX isoform and human progesterone receptor-A [PRA] isoform were obtained from Ligand Pharmaceuticals (San Diego, CA). Both receptor cDNAs were cloned into baculovirus expression vectors and expressed in insect SF21 cells. [ $^3$ H]-dexamethasone (Dex, specific activity 82-86 Ci/mmol) and [ $^3$ H]-progesterone (Prog, specific activity 97-102 Ci/mmol) were purchased from Amersham Life Sciences (Arlington Heights, IL). Glass fiber type C multiscreen MAFC NOB plates were from Millipore (Burlington, MA). Hydroxyapatite Bio-Gel HTP gel was from Bio-Rad Laboratories (Hercules, CA). Tris(hydroxymethyl)aminomethane (Tris), ethylenediaminetetraacetic acid (EDTA), glycerol, dithiothreitol (DTT) and sodium molybdate were obtained from Sigma Chemicals (St. Louis, MO). Microscint-20 scintillation fluid was from Packard Instrument (Meriden, CT).

Stock solutions (32 mM) of compounds were prepared in dimethylsulfoxide (DMSO), and 50X solutions of test compounds were prepared from the 32 mM solution with a 50:50 mixture of DMSO/ethanol. The 50X solution was then diluted with binding buffer that contained 10 mM Tri-HCl, 1.5 mM EDTA, 10% glycerol, 1 mM DTT, 20 mM sodium molybdate, pH 7.5 @ 4°C. 1% DMSO/ethanol was present in the binding assay.

GRX and PRA binding reactions were performed in Millipore Multiscreen plates. For GR binding assays, [<sup>3</sup>H]-Dex (~35,000 dpm (~0.9 nM)), GRX cytosol (~35 µg protein), test compounds and binding buffer were mixed in a total volume of 200 µL and incubated at 4 °C overnight in a plate shaker. Specific binding was defined as the difference between binding of [<sup>3</sup>H]Dex in the absence and in the presence of 1 µM unlabelled Dex.

For PR binding assays, [<sup>3</sup>H]Prog (~36,000 dpm (~0.8 nM)), PRA cytosol (~40 µg protein), test compounds and binding buffer were mixed in a total volume of 200 µL and incubated at 4 °C at overnight in a plate shaker. Specific binding was defined as the difference between binding of [<sup>3</sup>H]Prog in the absence and in the presence of 3 µM unlabelled Prog.

After an overnight incubation, 50 µL of hydroxyapatite (25 % weight/volume) slurry were added to each well and plates were incubated for 10 min at °C in a plate shaker. Plates were suctioned with a Millipore vacuum manifold and each well was rinsed with 300 µL of ice-cold binding buffer. A 250 µL aliquot of Packard Microscint-20 was added to each well and the wells were shaken at room temperature for 20 minutes. The amount of radioactivity was determined with a Packard TopCount plate reader.

#### Determination of Inhibition Constant (K<sub>i</sub>)

The concentration of test compounds that inhibited 50% of specific binding (IC<sub>50</sub>) was determined from a Hill analysis of the competitive binding experiments. The K<sub>i</sub> of test compounds was determined using the Cheng-Prusoff equation  $K_i = IC_{50} / (1 + [L^*] / [K_L])$  where L\* is the concentration of radioligand and K<sub>L</sub> is the dissociation constant of the radioligand determined from saturation analysis. For GRX, K<sub>L</sub> was ~1.5 nM, and for PRA, K<sub>L</sub> was ~4.5 nM. The inhibitory potencies of compounds of this invention and their selectivity for GR and PR receptors are shown in Table 1.

Table 1

| K <sub>i</sub> (nM) |
|---------------------|
|---------------------|

| Example Number | GR    | PR    |
|----------------|-------|-------|
| 1              | 8.6   | 10000 |
| 2              | 7.6   | 1702  |
| 3              | 4.8   | 2654  |
| 4              | 7     | 2960  |
| 5              | 357.5 | 10000 |
| 6              | 3.8   | 321   |
| 7              | 4.3   | 5676  |
| 8              | 167.9 | 6007  |
| 9              | 60.5  | 10000 |
| 10             | 179.1 | 10925 |
| 11             | 4.4   | 288   |
| 12             | 8.6   | 10000 |
| 13             | 11.1  | 10000 |
| 14             | 5.2   | 10000 |
| 15             | 2.5   | 10000 |
| 16             | 8     | 10000 |
| 17             | 39    | 10000 |
| 18             | 10.5  | 1035  |
| 19             | 6.7   | 4967  |
| 20             | 3.7   | 1684  |
| 21             | 10.7  | 4017  |
| 22             | 6.5   | 10000 |
| 23             | 8.2   | 6153  |
| 24             | 3.5   | 14837 |
| 25             | 240.4 | 10000 |
| 26             | 2.1   | 13390 |
| 27             | 5.2   | 3580  |
| 28             | 4.7   | 3271  |
| 29             | 7.7   | 7763  |
| 30             | 13    | 7924  |
| 31             | 12.2  | 10000 |
| 32             | 3.3   | 1559  |
| 33             | 95.2  | 8318  |
| 34             | 4     | 4706  |

|    |      |       |
|----|------|-------|
| 35 | 260  | 10000 |
| 36 | 1.4  | 1704  |
| 37 | 20   | 10000 |
| 38 | 207  | 10000 |
| 39 | 31   | 10000 |
| 40 | 18   | 18132 |
| 41 | 9.5  | 3303  |
| 42 | 99   | 10000 |
| 43 | 72   | 10000 |
| 44 | 190  | 19524 |
| 45 | 15   | 10000 |
| 46 | 2.7  | 3436  |
| 47 | 174  | 10000 |
| 48 | 5.8  | 2769  |
| 49 | 13   | 10000 |
| 50 | 4.9  | 9449  |
| 51 | 18   | 7333  |
| 52 | 3    | 2269  |
| 53 | 8.1  | 2912  |
| 54 | 6.6  | 7344  |
| 55 | 8.2  | 10000 |
| 56 | 6.2  | 10000 |
| 57 | 50   | 4275  |
| 58 | 9    | 8572  |
| 59 | 9.5  | 16582 |
| 60 | 14   | 10493 |
| 61 | 62   | 14393 |
| 62 | 12   | 10000 |
| 63 | 511  | 10000 |
| 64 | 62   | 1671  |
| 65 | 591  | 10000 |
| 66 | 2.7  | 502   |
| 67 | 21.7 | 10000 |
| 68 | 8    | 9054  |
| 69 | 15   | 17331 |
| 70 | 25.5 | 7301  |

|     |       |        |
|-----|-------|--------|
| 71  | 7.7   | 484    |
| 72  | 17.8  | 1454   |
| 73  | 10.3  | 4500   |
| 74  | 11.9  | 4877   |
| 75  | 7.3   | 13800  |
| 76  | 152   | 10000  |
| 77  | 1.6   | 173    |
| 78  | 80.5  | 10000  |
| 79  | 19.2  | 10000  |
| 80  | 168.2 | 10000  |
| 81  | 155.3 | 10000  |
| 82  | 22.9  | 327    |
| 83  | 54.8  | 2210   |
| 84  | 17.3  | 10000  |
| 85  | 3.5   | 10000  |
| 86  | 2.1   | 10000  |
| 87  | 4.7   | 10000  |
| 88  | 6     | 15327  |
| 89  | 275   | 10000  |
| 90  | 7.6   | 10000  |
| 91  | 17    | 10000  |
| 92  | 12    | 10000  |
| 93  | 148   | 10000  |
| 94  | 43    | 10000  |
| 95  | 31    | 10000  |
| 96  | 10    | 9163   |
| 97  | 320   | 10000  |
| 98  | 9.8   | 10000  |
| 99  | 3.6   | 10000  |
| 100 | 7.8   | 10000  |
| 101 | 11.4  | 10000  |
| 102 | 17.7  | 10000  |
| 103 | 5.2   | 10000  |
| 104 | 8.9   | 10000  |
| 105 | 9     | >10000 |
| 106 | 62    | >10000 |

|     |      |        |
|-----|------|--------|
| 107 | 215  | >10000 |
| 108 | 638  | >10000 |
| 109 | 6.1  | 10000  |
| 110 | 5.6  | 10000  |
| 111 | 7.2  | 10000  |
| 112 | 31   | 10000  |
| 113 | 9.7  | 10000  |
| 114 | 12   | 10000  |
| 115 | 17   | 10000  |
| 116 | 7.2  | 10000  |
| 117 | 12   | 10000  |
| 118 | 43   | 10000  |
| 119 | 6.9  | 10000  |
| 120 | 30.3 | 6235   |
| 121 | 11.3 | 672    |
| 122 | 11.8 | 1409   |
| 123 | 6.1  | 9568   |
| 124 | 3.2  | 1611   |
| 125 | 36.6 | 10000  |
| 126 | 2.9  | 1407   |
| 127 | 29.3 | 10000  |
| 128 | 5.9  | 10000  |
| 129 | 5.5  | 3621   |
| 130 | 11.9 | 1054   |
| 131 | 7.71 | 996    |
| 132 | 230  | 9890   |
| 133 | 3.6  | 4867   |
| 134 | 238  | 10000  |
| 135 |      |        |
| 136 | 37   | 2700   |
| 137 | 5.5  | 2410   |
| 138 | 2.2  | 5600   |
| 139 | 235  | 4800   |
| 140 | 13   | 10000  |
| 141 | 10   | 10000  |
| 142 | 51   | 10000  |

|     |      |        |
|-----|------|--------|
| 143 | 91   | 8100   |
| 144 | 7.7  | 10000  |
| 145 | 78   | 10000  |
| 146 | 8.3  | 8300   |
| 147 | 15   | 9300   |
| 148 | 2.8  | 10000  |
| 149 | 2.7  | 4063   |
| 150 | 106  | 10000  |
| 151 | 298  | 10000  |
| 152 | 1.8  | 10000  |
| 153 | 1.9  | 10000  |
| 154 | 0.7  | 10000  |
| 155 | 0.86 | 10000  |
| 156 | 0.9  | 4100   |
| 157 | 1.5  | 433    |
| 158 | 48   | 10000  |
| 159 | 3.8  | 1837   |
| 160 | 1.8  | 10000  |
| 161 | 3.3  | 10000  |
| 162 | 6.5  | 10000  |
| 163 | 2.6  | 10000  |
| 164 | 36   | 10000  |
| 165 | 14   | 10000  |
| 166 | 8.16 | 5631   |
| 167 | 21   | 10000  |
| 168 | 2.5  | 10000  |
| 169 | 300  | 10000  |
| 170 | 82   | 10000  |
| 171 | 3.3  | 7429   |
| 172 | 7    | 9900   |
| 173 | 32   | 10000  |
| 174 | 270  | 10000  |
| 175 | 44   | 7700   |
| 176 | 88   | >10000 |
| 178 | 468  | 10000  |
| 179 | 9.5  | 2750   |

|      |      |       |
|------|------|-------|
| 180  | 18   | 733   |
| 181  | 207  | 10000 |
| 182  | 23   | 10000 |
| 183  | 38   | 10000 |
| 184  | 40   | 10000 |
| 185  | 288  | 10000 |
| 186  | 90   | 10000 |
| 187  | 46   | 3900  |
| 188  | 4.9  | 5300  |
| 189  | 6.4  | 1700  |
| 190  | 6.25 | 1586  |
| 191  | 2.9  | 1190  |
| 192  | 3.1  | 10000 |
| 193  | 2.0  | 2184  |
| 194  | 7.7  | 10000 |
| 195  | 25   | 10000 |
| 196  |      |       |
| 197  | 28   | 10000 |
| 198  | 0.65 | 2130  |
| 199  | 106  | 10000 |
| 200  | 45   | 10000 |
| 201  | 114  | 10000 |
| 202  | 134  | 10000 |
| 203  | 85   | 10000 |
| 204  | 74   | 10000 |
| 205  | 11.4 | 10000 |
| 206  | 201  | 10000 |
| 206A | 4192 |       |
| 207  | 22   | 10000 |
| 208  | 25   | 970   |
| 209  | 2.0  | 5462  |
| 210  | 21   | 710   |
| 211  | 5.3  | 10000 |
| 212  | 13   | 10000 |
| 213  | 67   | 10000 |
| 214  | 5.7  | 10000 |

|     |      |       |
|-----|------|-------|
| 215 | 20   | 10000 |
| 216 | 0.58 | 7.6   |
| 217 | 1    | 65.1  |
| 218 | 1.6  | 227   |
| 219 | 2.4  | 178   |
| 220 | 0.66 | 527   |
| 221 | 0.66 | 4.2   |
| 222 | 0.47 | 9.9   |
| 223 | 2.6  | 297   |
| 224 | 57   | 786   |
| 225 | 155  | 5010  |
| 226 | 2.6  | 220   |
| 227 | 8.4  | 1930  |
| 228 | 5.4  | 29.5  |
| 229 | 34.7 | 1338  |
| 230 | 2.4  | 50.3  |
| 231 | 30.2 | 1870  |
| 232 | 1.6  | 230   |
| 233 | 2.5  | 350   |
| 234 | 3.8  | 202   |
| 235 | 0.94 | 155   |
| 236 | 0.89 | 36.2  |
| 237 | 1.5  | 18    |
| 238 | 1.2  | 11.5  |
| 239 | 16.8 | 240   |
| 240 | 52.2 | 2173  |
| 241 | 0.69 | 61.1  |
| 242 | 0.53 | 3420  |
| 243 | 1.6  | 21.2  |
| 244 | 6.3  | 804   |
| 245 | 0.95 | 119   |
| 246 | 0.87 | 113   |
| 247 | 0.86 | 195   |
| 248 | 1    | 870   |
| 249 | 0.80 | 488   |
| 250 | 2.4  | 1475  |

|     |      |       |
|-----|------|-------|
| 251 | 0.87 | 163   |
| 252 | 0.39 | 102   |
| 253 | 0.38 | 42    |
| 254 | 2.2  | 1824  |
| 255 | 1.5  | 1434  |
| 256 | 3.8  | 266   |
| 257 | 10   | 1624  |
| 258 | 10.7 | 879   |
| 259 | 1.2  | 938   |
| 260 | 3.3  | 250   |
| 261 | 0.75 | 161   |
| 262 | 1.1  | 150   |
| 263 | 2.2  | 59.6  |
| 264 | 0.51 | 307   |
| 265 | 767  | 1499  |
| 266 | 0.71 | 102   |
| 267 | 0.79 | 938   |
| 268 | 0.84 | 486   |
| 269 | 17.1 | 2467  |
| 270 | 0.66 | 4756  |
| 271 | 0.82 | 2288  |
| 272 | 0.39 | 66.4  |
| 273 | 0.56 | 35.8  |
| 274 | 0.69 | 386   |
| 275 | 11.7 | 2873  |
| 276 |      |       |
| 277 | 11.3 | 272   |
| 278 | 1.1  | 533   |
| 279 | 12.4 | 1900  |
| 280 | 1.6  | 10000 |
| 281 | 0.84 | 526   |
| 282 | 0.5  | 42    |
| 283 | 1.1  | 60.4  |
| 284 | 110  | 2097  |
| 285 | 436  | 3757  |
| 286 | 64   | 3029  |

|     |      |       |
|-----|------|-------|
| 287 | 346  | 3502  |
| 288 | 0.86 | 4080  |
| 289 | 0.73 | 260   |
| 290 | 12.1 | 611   |
| 291 | 8.1  | 592   |
| 292 | 487  | 8338  |
| 293 | 12   | 3742  |
| 294 | 13.8 | 1807  |
| 295 | 0.67 | 59.3  |
| 296 | 0.63 | 476   |
| 297 | 4.7  | 4844  |
| 298 | 4.1  | 10000 |
| 298 | 4.1  | 10000 |
| 299 | 5.4  | 2900  |
| 300 | 5.3  | 34.4  |
| 301 | 16   | 113   |
| 302 | 5.9  | 99    |
| 303 | 4.9  | 58.5  |
| 304 | 34.5 | 681   |
| 305 | 2    | 6919  |
| 306 | 717  | 4455  |
| 307 | 4.6  | 27.8  |
| 308 | 50.8 | 960   |
| 309 | 1.9  | 60.7  |
| 310 | 4.4  | 382   |
| 311 | 15   | 10000 |
| 312 | 8.4  | 10000 |
| 313 | 6.4  | 10000 |
| 314 | 1.7  | 10000 |
| 315 | 13   | 10000 |
| 316 | 11   | 10000 |
| 317 | 6.5  | 10000 |
| 318 | 553  | 10000 |
| 319 | 16   | 492   |
| 320 | 49   | 3050  |
| 321 | 44   | 2880  |

|     |      |       |
|-----|------|-------|
| 322 | 107  | 2300  |
| 323 | 428  | 10000 |
| 324 | 24   | 10000 |
| 325 | 24   | 10000 |
| 326 | 228  | 10000 |
| 327 | 9.3  | 1457  |
| 329 | 2.2  | 192   |
| 330 | 2.2  | 53    |
| 331 | 142  | 10000 |
| 332 | 18   | 10000 |
| 333 | 5.6  | 3670  |
| 334 | 9.5  | 10000 |
| 335 | 652  | 10000 |
| 336 | 9.5  | 1564  |
| 337 | 3.3  | 702   |
| 338 | 61   | 10000 |
| 339 | 112  | 10000 |
| 340 | 1.8  | 254   |
| 341 | 2.5  | 10000 |
| 342 | 2586 | 10000 |
| 343 | 5.2  | 4700  |
| 344 | 0.46 | 76.7  |
| 345 | 8.7  | 3000  |
| 346 | 44   | 5110  |
| 347 | 128  | 10000 |
| 348 | 0.89 | 171   |
| 349 | 10.5 | 10000 |
| 350 | 6.22 | 10000 |
| 351 | 93   | 10000 |
| 352 | 58   | 10000 |
| 353 | 20   | 10000 |
| 354 | 32   | 1500  |
| 355 | 27   | 4280  |
| 356 | 15   | 2968  |
| 357 | 59.8 | 10000 |
| 358 | 4.2  | 8963  |

|     |      |       |
|-----|------|-------|
| 359 | 11.3 | 2219  |
| 360 | 33.7 | 10000 |
| 361 | 95.7 | 9143  |
| 362 | 6.5  | 3370  |
| 363 | 5    | 3942  |
| 364 | 424  | 10000 |
| 365 | 2.2  | 98    |
| 366 | 2.1  | 83.9  |
| 367 | 2.2  | 7.6   |
| 368 | 0.21 | 61    |
| 369 | 0.41 | 2528  |

|     |      |       |
|-----|------|-------|
| 372 | 1.8  | 164   |
| 373 | 3.1  | 279   |
| 374 | 9.0  | 222   |
| 375 | 3    | 1093  |
| 376 | 0.78 | 156   |
| 377 | 51   | 3085  |
| 378 | 1.1  | 440   |
| 379 | 1.4  | 175   |
| 380 | 1.2  | 204   |
| 381 | 7.1  | 9825  |
| 382 | 2.2  | 150   |
| 383 | 4.8  | 46    |
| 384 | 0.67 | 197   |
| 385 | 0.9  | 170   |
| 386 | 6.5  | 105   |
| 387 | 0.65 | 169   |
| 388 | 2.8  | 199   |
| 389 | 0.58 | 27.5  |
| 390 | 0.96 | 520   |
| 391 | 1.7  | 1087  |
| 392 | 1.2  | 487   |
| 393 | 0.76 | 589   |
| 394 | 0.89 | 109   |
| 395 | 2.1  | 1213  |
| 396 | 6.3  | 2125  |
| 397 | 2.3  | 22.8  |
| 398 | 6.7  | 1085  |
| 399 | 24.4 | 10000 |
| 400 | 3.5  | 5962  |
| 401 | 134  | 6083  |
| 402 | 3.3  | 10063 |
| 403 | 131  | 10000 |
| 404 | 1.3  | 49.7  |
| 405 | 1.1  | 75.1  |
| 406 | 2.3  | 97.9  |

|     |      |       |
|-----|------|-------|
| 407 | 1.8  | 16.4  |
| 408 | 112  | 14138 |
| 409 | 2.7  | 42    |
| 410 | 1.1  | 25.7  |
| 411 | 0.68 | 8.4   |
| 412 | 9    | 222   |
| 413 | 0.22 | 60.8  |
| 414 | 93.2 | 21805 |
| 415 | 9.9  | 3741  |
| 416 | 3.1  | 394   |
| 417 | 3    | 10.5  |
| 418 | 1.4  | 2.1   |
| 419 | 56.9 | 286   |
| 420 | 125  | 2396  |
| 421 | 0.66 | 11.6  |
| 422 | 0.28 | 2.9   |
| 423 | 0.67 | 8184  |
| 424 | 0.84 | 1952  |
| 425 | 0.35 | 3942  |
| 426 | 0.85 | 110   |
| 427 | 7.8  | 2205  |
| 428 | 0.91 | 204   |
| 429 | 4.1  | 29.1  |
| 430 | 4.8  | 281   |
| 431 | 113  | 10000 |
| 432 | 1.4  | 207   |
| 433 | 30.2 | 1413  |
| 434 | 0.96 | 123   |
| 435 | 120  | 734   |
| 436 | 18.8 | 5919  |
| 437 | 0.97 | 449   |
| 438 | 0.89 | 129   |
| 439 | 1.2  | 202   |
| 440 | 0.70 | 390   |
| 441 | 0.42 | 328   |
| 442 | 9.1  | 8863  |

|     |      |       |
|-----|------|-------|
| 443 | 63.5 | 10000 |
| 444 | 1.6  | 406   |
| 445 | 4    | 347   |

The present invention also provides pharmaceutical compositions which comprise compounds of the present invention formulated together with one or more non-toxic pharmaceutically acceptable carriers. The pharmaceutical compositions may be specially formulated for oral administration in solid or liquid form, for parenteral injection, or for rectal administration.

The pharmaceutical compositions of this invention can be administered to humans and other animals orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically (as by powders, ointments, or drops), buccally, or as an oral or nasal spray. The term "parenteral" administration refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

Pharmaceutical compositions of this invention for parenteral injection comprise pharmaceutically acceptable sterile aqueous or nonaqueous solutions, dispersions, suspensions or emulsions as well as sterile powders for reconstitution into sterile injectable solutions or dispersions just prior to use. Examples of suitable aqueous and nonaqueous carriers, diluents, solvents or vehicles include water, ethanol, polyols (such as glycerol, propylene glycol, polyethylene glycol, and the like), and suitable mixtures thereof, vegetable oils (such as olive oil), and injectable organic esters such as ethyl oleate. Proper fluidity can be maintained, for example, by the use of coating materials such as lecithin, by the maintenance of the required particle size in the case of dispersions, and by the use of surfactants. Conversely, reduced particle size may maintain biological activity.

These compositions may also contain adjuvants such as preservative, wetting agents, emulsifying agents, and dispersing agents. Prevention of the action of microorganisms may be ensured by the inclusion of various antibacterial and antifungal agents, for example, paraben, chlorobutanol, phenol sorbic acid, and the like. It may also be desirable to include isotonic agents such as sugars, sodium chloride, and the like. Prolonged absorption of the injectable pharmaceutical form may be brought about by the inclusion of agents which delay absorption such as aluminum monostearate and gelatin.

In some cases, in order to prolong the effect of the drug, it is desirable to slow the absorption of the drug from subcutaneous or intramuscular injection. This may be accomplished by the use of a liquid suspension of crystalline or amorphous material with poor water solubility. The rate of absorption of the drug then depends upon its rate of dissolution which, in turn, may depend upon crystal size and crystalline form.

Alternatively, delayed absorption of a parenterally administered drug form is accomplished by dissolving or suspending the drug in an oil vehicle.

Injectable depot forms are made by forming microencapsule matrices of the drug in biodegradable polymers such as polylactide-polyglycolide. Depending upon the ratio of drug to polymer and the nature of the particular polymer employed, the rate of drug release can be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations are also prepared by entrapping the drug in liposomes or microemulsions which are compatible with body tissues.

The injectable formulations can be sterilized, for example, by filtration through a bacterial-retaining filter, or by incorporating sterilizing agents in the form of sterile solid compositions which can be dissolved or dispersed in sterile water or other sterile injectable medium just prior to use.

Solid dosage forms for oral administration include capsules, tablets, pills, powders, and granules. In such solid dosage forms, the active compound is mixed with at least one inert, pharmaceutically acceptable excipient or carrier such as sodium citrate or dicalcium phosphate and/or a) fillers or extenders such as starches, lactose, sucrose, glucose, mannitol, and silicic acid, b) binders such as, for example, carboxymethylcellulose, alginates, gelatin, polyvinylpyrrolidone, sucrose, and acacia, c) humectants such as glycerol, d) disintegrating agents such as agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates, and sodium carbonate, e) solution retarding agents such as paraffin, f) absorption accelerators such as quaternary ammonium compounds, g) wetting agents such as, for example, cetyl alcohol and glycerol monostearate, h) absorbents such as kaolin and bentonite clay, and i) lubricants such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, and mixtures thereof. In the case of capsules, tablets and pills, the dosage form may also comprise buffering agents.

Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugar as well as high molecular weight polyethylene glycols and the like.

The solid dosage forms of tablets, dragees, capsules, pills, and granules can be prepared with coatings and shells such as enteric coatings and other coatings well known in the pharmaceutical formulating art. They may optionally contain opacifying agents and can also be of a composition that they release the active ingredient(s) only, or preferentially, in a certain part of the intestinal tract, optionally, in a delayed manner. Examples of embedding compositions which can be used include polymeric substances and waxes.

The active compounds can also be in micro-encapsulated form, if appropriate, with one or more of the above-mentioned excipients.

Liquid dosage forms for oral administration include pharmaceutically acceptable emulsions, solutions, suspensions, syrups and elixirs. In addition to the active compounds, the liquid dosage forms may contain inert diluents commonly used in the art such as, for example, water or other solvents, solubilizing agents and emulsifiers such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, dimethyl formamide, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor, and sesame oils), glycerol, tetrahydrofurfuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan, and mixtures thereof.

Besides inert diluents, the oral compositions can also include adjuvants such as wetting agents, emulsifying and suspending agents, sweetening, flavoring, and perfuming agents.

Suspensions, in addition to the active compounds, may contain suspending agents as, for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar, and tragacanth, and mixtures thereof.

Compositions for rectal or vaginal administration are preferably suppositories which can be prepared by mixing the compounds of this invention with suitable non-irritating excipients or carriers such as cocoa butter, polyethylene glycol or a suppository wax which are solid at room temperature but liquid at body temperature and therefore melt in the rectum or vaginal cavity and release the active compound.

Compounds of the present invention can also be administered in the form of liposomes. As is known in the art, liposomes are generally derived from phospholipids or other lipid substances. Liposomes are formed by mono- or multi-lamellar hydrated liquid crystals that are dispersed in an aqueous medium. Any non-toxic, physiologically acceptable and metabolizable lipid capable of forming liposomes can be used. The present compositions in liposome form can contain, in addition to a compound of the present invention, stabilizers, preservatives, excipients, and the like. The preferred lipids are the phospholipids and the phosphatidyl cholines (lecithins), both natural and synthetic.

Methods to form liposomes are known in the art. See, for example, Prescott, Ed., Methods in Cell Biology, Volume XIV, Academic Press, New York, N.Y. (1976), p. 33 et seq.

Dosage forms for topical administration of a compound of this invention include powders, sprays, ointments and inhalants. The active compound is mixed under sterile conditions with a pharmaceutically acceptable carrier and any needed preservatives,

buffers, or propellants which may be required. Ophthalmic formulations, eye ointments, powders and solutions are also contemplated as being within the scope of this invention.

Actual dosage levels of active ingredients in the pharmaceutical compositions of this invention may be varied so as to obtain an amount of the active compound(s) that is effective to achieve the desired therapeutic response for a particular patient, compositions, and mode of administration. The selected dosage level will depend upon the activity of the particular compound, the route of administration, the severity of the condition being treated, and the condition and prior medical history of the patient being treated. However, it is within the skill of the art to start doses of the compound at levels lower than required for to achieve the desired therapeutic effect and to gradually increase the dosage until the desired effect is achieved.

Generally dosage levels of about 1 to about 50, more preferably of about 5 to about 20 mg of active compound per kilogram of body weight per day are administered orally to a mammalian patient. If desired, the effective daily dose may be divided into multiple doses for purposes of administration, e.g. two to four separate doses per day.

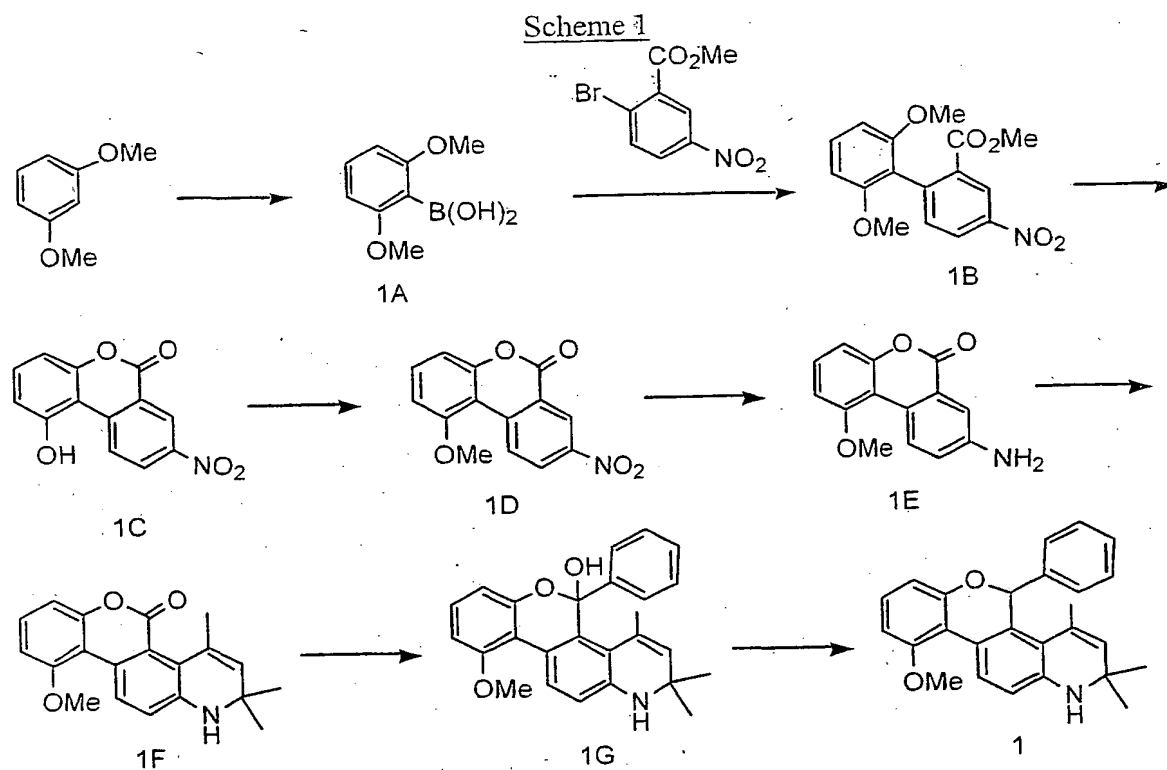
#### Abbreviations

Abbreviations that have been used in the descriptions of the scheme and the examples that follow are:  $\text{BF}_3 \cdot \text{OEt}_2$  for boron trifluoride diethyl ether complex; DMF for N,N-dimethylformamide, DMSO for dimethylsulfoxide; and THF for tetrahydrofuran.

#### Synthetic Methods

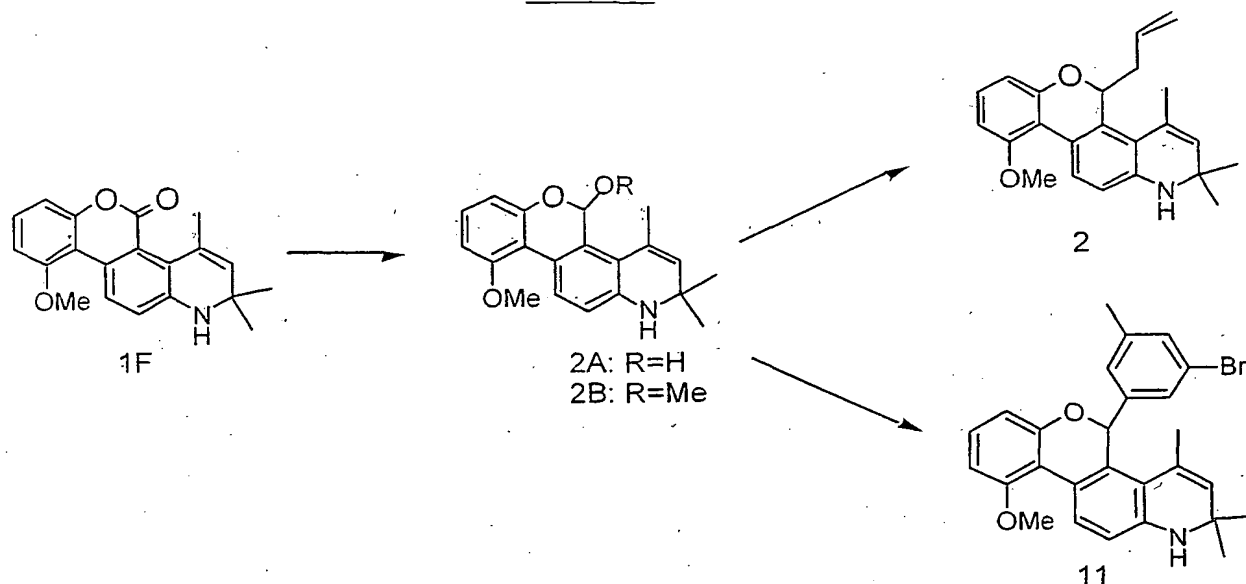
The compounds and processes of the present invention will be better understood in connection with the following synthetic schemes which illustrate the methods by which the compounds of the invention can be prepared.

Syntheses of the compounds of the present invention are described in Schemes 1-21.



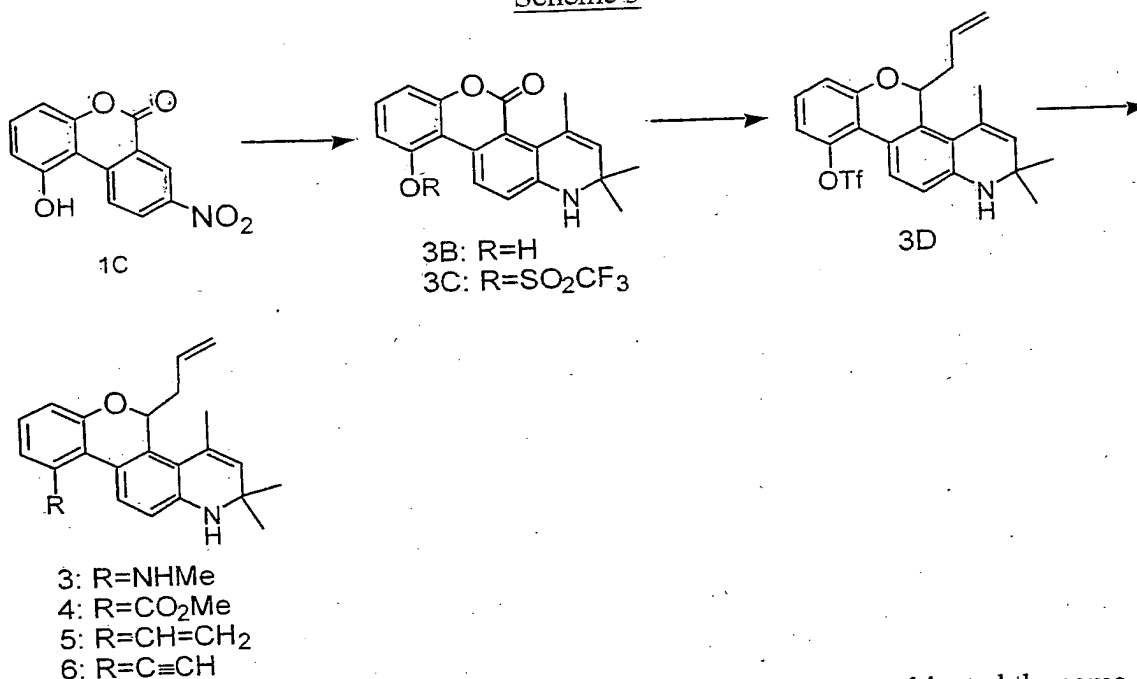
As exemplified in Scheme 1, resorcinol dimethyl ether was metallated with a strong base such as *n*- or *sec*-butyllithium, treated with a trialkoxyborate such as trimethyl- or triisopropylborate and hydrolyzed with acid such as 2M HCl to provide boronic acid **1A**. Treatment of **1A** with methyl 5-nitro-2-bromobenzoate in the presence of a palladium catalyst such as tetrakis(triphenylphosphine)palladium(0) or dichlorobis(triphenylphosphine)palladium (II) provided biphenyl **1B**. Demethylation of **1B** was accomplished with reagents such as BBr<sub>3</sub>, to provide hydroxylactone **1C**, which was treated with alkylating agents such as methyl iodide to provide **1D**. Conversion of **1D** to amine **1E** was accomplished using hydrogen gas and a palladium catalyst such as 10% palladium on carbon. **1E** was converted to quinoline **1F** by a Skraup ring annulation reaction. Introduction of functionalization at the C-5 position of **1F** to provide **1** was achieved through addition of organometallic reagents such as phenyllithium to the C-5 carbonyl to provide **1G**, followed by deoxygenation with Lewis acids such as BF<sub>3</sub>·OEt<sub>2</sub> and reducing agents such as triethylsilane to provide **1**.

Scheme 2



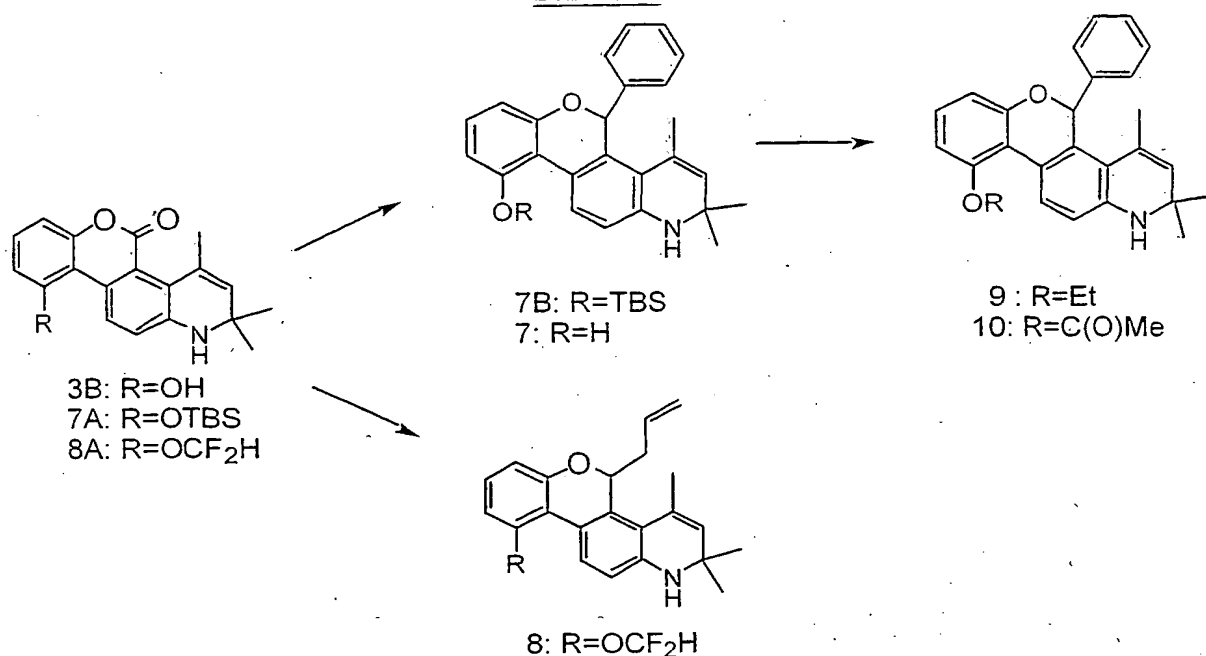
A more preferred route to compounds of this invention is exemplified in Scheme 2. 1F was converted to methyl acetal 2B, via hemiacetal 2A, using a two-step procedure comprising conversion of 1F to 2A with reagents such as diisobutylaluminum hydride in an aprotic solvent such as dichloromethane followed by acid-catalyzed acetal formation with acids such as p-toluenesulfonic acid monohydrate and alcohols such as methanol to provide 2B. 2B was treated with nucleophiles such as allyltrimethylsilane in the presence of a Lewis acid such as boron trifluoride diethyl etherate to form C-5 allyl analogs such as Example 2. The Lewis acid/methyl acetal complex was also condensed with organomagnesium chlorides, bromides or iodides to provide compounds of this invention such as Example 11.

Scheme 3



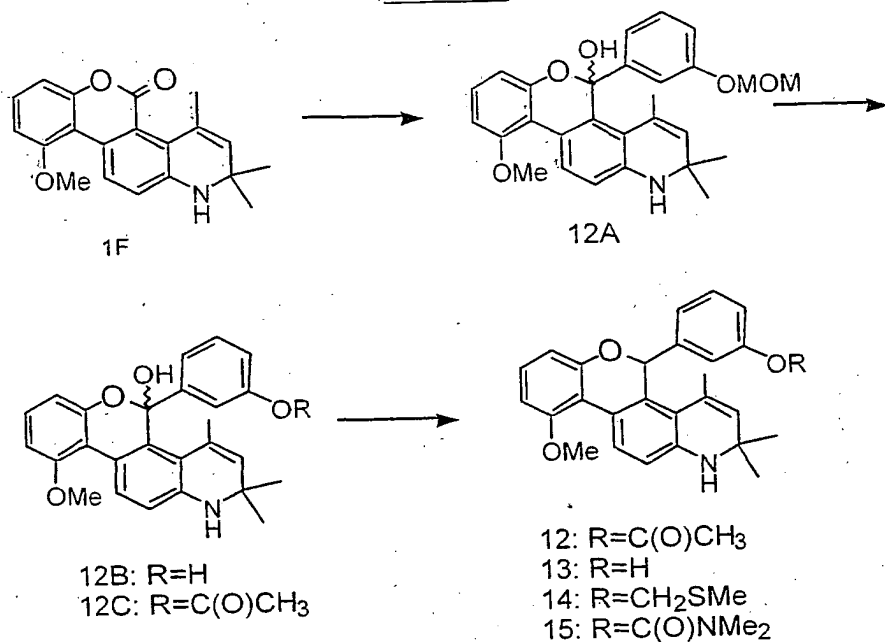
As exemplified in Scheme 3, the C-10 position of 1C was subjected the same reduction/Skraup conditions described in Scheme 1 to afford hydroxyquinoline 3B. 3B was converted to triflate derivative 3C with reagents such as trifluoromethanesulfonic anhydride then derivatized at the C-5 position as described in schemes 1 and 2 to provide analogs such as 3D. The functionalized C-10 triflates were used in coupling reactions mediated by palladium catalysts for aminations, carbonylations, Stille couplings and modified Sonagashira reactions and provided aminomethyl, carbomethoxy, vinyl and acetylenic derivatives of 3D such as the C-5 allyl-substituted examples 3, 4, 5, and 6, respectively.

Scheme 4



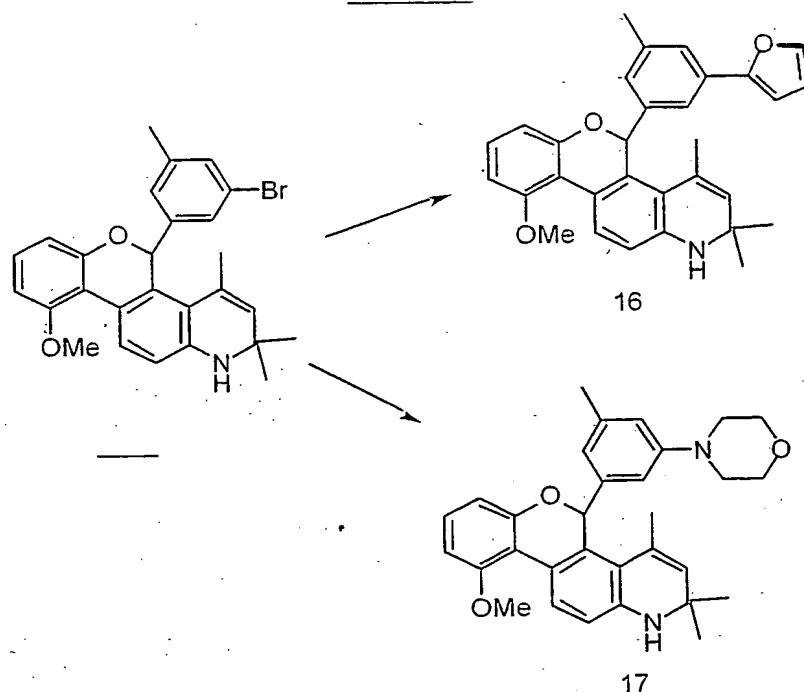
As shown in Scheme 4, treatment of 3B with *tert*-butyl dimethylsilyl (TBS) ether and a base such as imidazole, triethylamine or diisopropylethylamine and functionalization of the C-5 position as described in schemes 1-3 provided silane 7B. Removal of the silane group with reagents such as tetra n-butylammonium fluoride in THF, to provide phenol 7, and treatment with R-X or RC(O)X, where R is an alkyl group and X is a leaving group such as halogen, provided alkoxy and carboxy compounds such as examples 9 and 10. Halo alkoxy analogs were prepared from 3B by nucleophilic displacement using a polyhalogenated alkylating agent such as CF<sub>2</sub>HCl to provide 8A followed by functionalization at the C-5 position of 8A, as described in Schemes 1-3, to provide 8.

Scheme 5



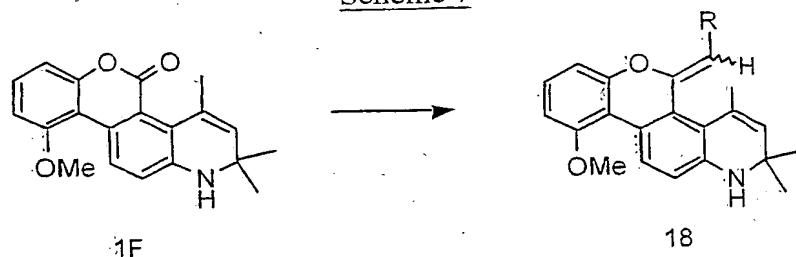
As exemplified in Scheme 5, 1F was treated with lithiated, O-protected phenol reagents, such as 3-(methoxymethoxy)phenyllithium, to provide 12A. The protecting group was cleaved in acidic media, such as methanolic or aqueous HCl, to provide diol 12B which was converted to phenyl acetates 12C with reagents such as acetyl chloride and base such as pyridine, triethylamine or diisopropylethylamine. The tertiary alcohol was then reduced as described in Scheme 1, and the acetate group of Example 12 was removed to provide Example 13. Example 13 was alkylated or acylated as described in Scheme 4 to provide examples 14 and 15.

Scheme 6



As shown in Scheme 6, functionality in the meta position of the phenyl ring in the C-5 position was introduced using meta-halophenyl analogs such as Example 11, prepared as described in Scheme 2. Stille or Suzuki couplings or aminations with palladium catalysts such as [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium(II) or tetrakis(triphenylphosphine)palladium(0) in the presence of ligands such as tributylstannylfuran or morpholine provided carbon- or nitrogen-bound groups in the meta position of the aromatic ring at the C-5 position as exemplified in examples 16 and 17, respectively.

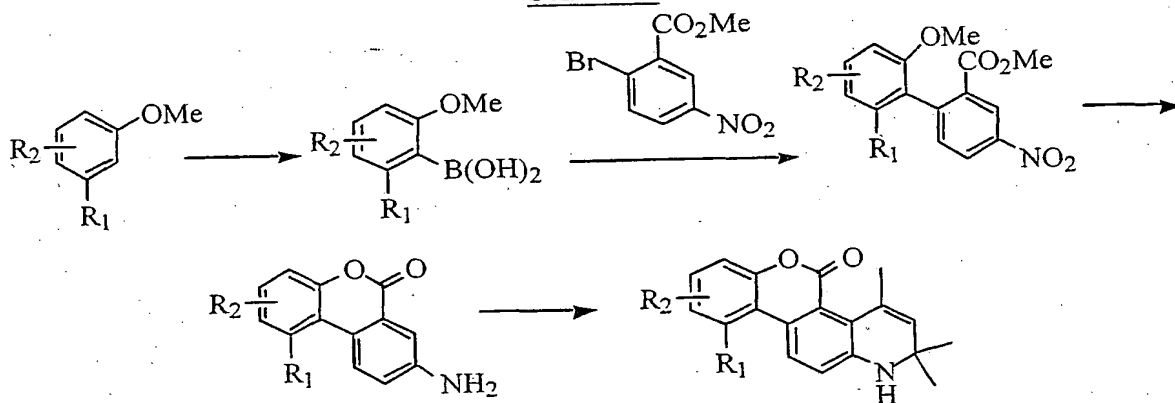
Scheme 7



As shown in Scheme 7, 1F was treated with magnesium halides, preferably bromides, to provide an intermediate hemiketal which was treated with acid catalysts such as para-toluenesulfonic acid, methanesulfonic acid or aqueous hydrochloric acid to provide optionally substituted analogs such as 18 as mixtures of E and Z isomers.

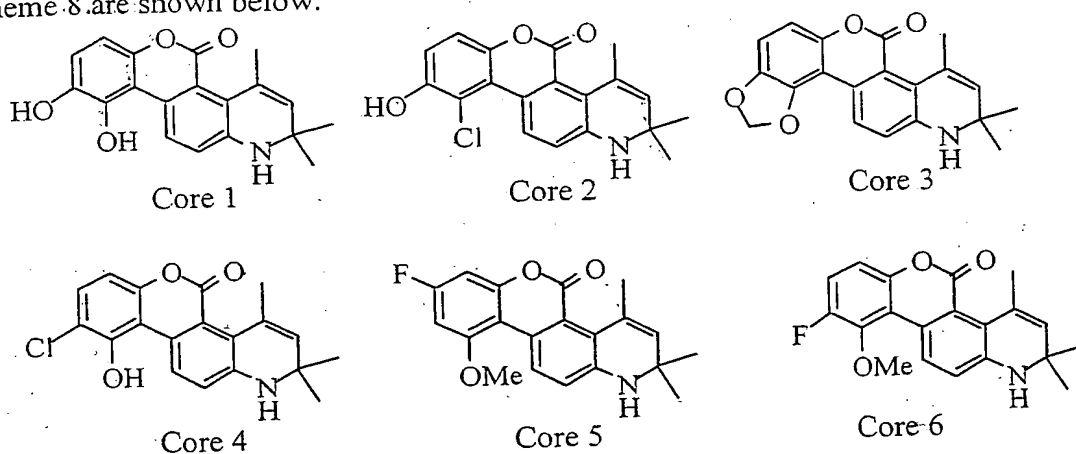
The chemistry shown in Scheme 1 was found to be general. Thus, a variety of tetracyclic cores could be prepared from an assortment of substituted anisoles via their corresponding boronic acids according to Scheme 8.

Scheme 8

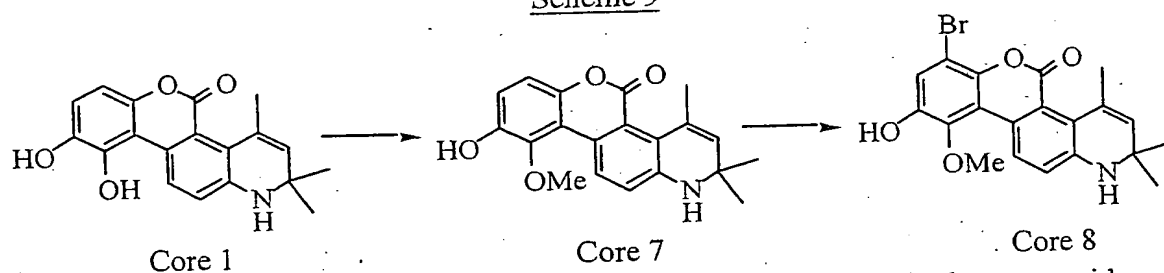


Scheme 8 shows the applicability of the chemistry described in Scheme 1 and Examples 1-131 to the synthesis of new cores with substituents other than alkoxy at the C-10 position. Ortho metallation of substituted anisoles with a strong base such as n- or sec-butyllithium, followed by sequential treatment with a trialkoxyborate such as trimethyl- or triisopropylborate and hydrolysis with acid, as described in Scheme 1, provided the appropriately substituted boronic acids which were then elaborated to compounds of Formula I using chemistry described above. Further elaboration of the ring to provide Cores 1-17 is described below.

Examples of novel tetracyclic cores prepared using the chemistry described in Scheme 8 are shown below.

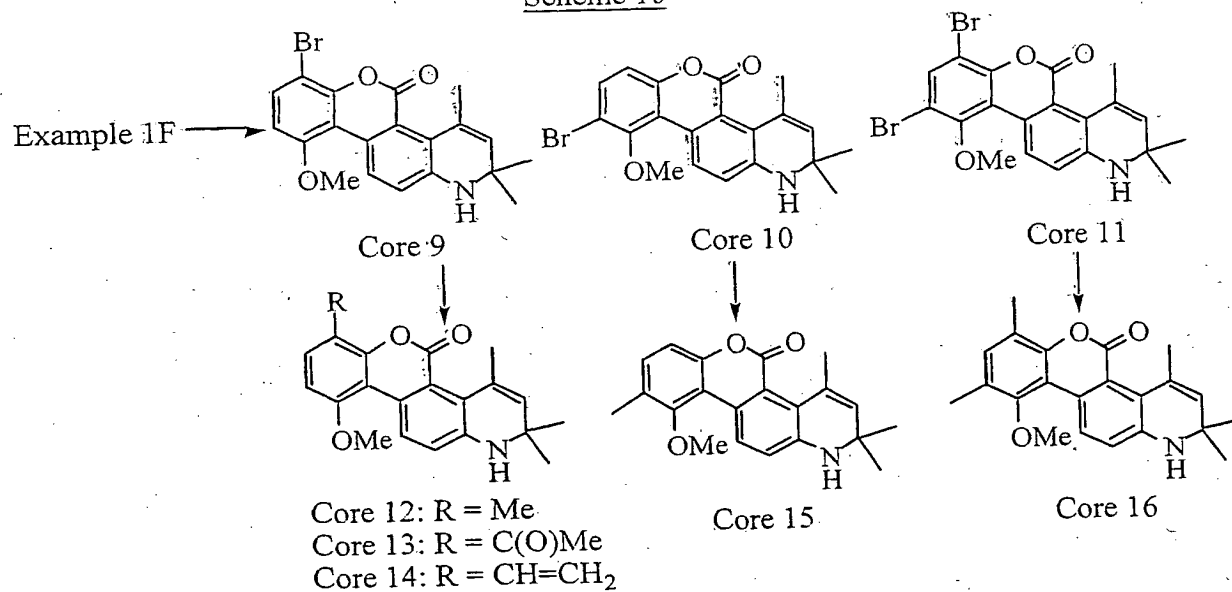


Scheme 9



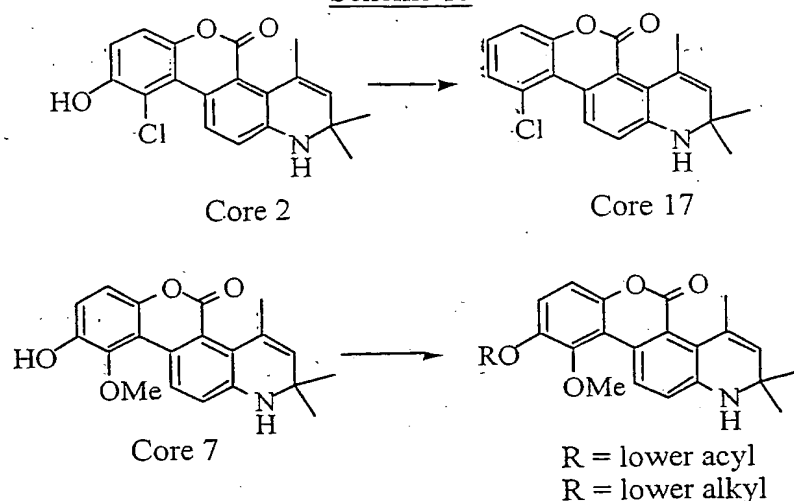
Further derivatization of Core 1 using methods well-known in the art provide additional tetracyclic coumarins for subsequent elaboration at the C-5 position, as shown in Scheme 9. For example, selective alkylation of the C-10 hydroxyl of Core 1 with alkylating agents (e.g., methyl iodide) and base, such as potassium carbonate, provided Core 7. Selective derivitization of Core 1 at the C-7 position with halogenating agents such as bromine or N-bromosuccinimide provided the compound of Formula I precursor Core 8.

Scheme 10



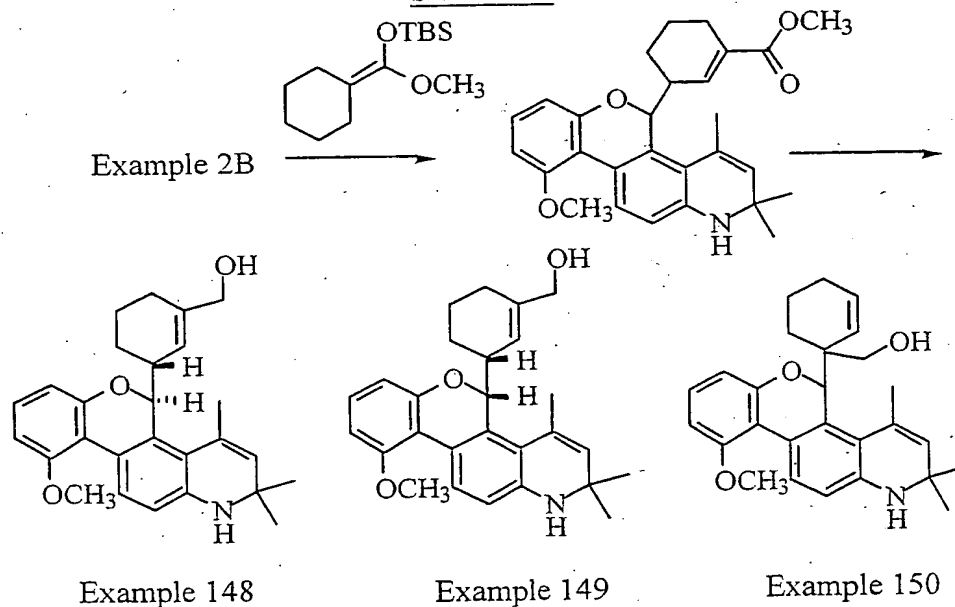
5 Scheme 10 shows additional selective bromination chemistry. Regiochemical bromination of Example 1F, as directed by the C-10 methoxy group and choice of brominating agent, provided Cores 9, 10, and 11. These brominated rings were further derivatized at the brominated position(s) by transition metal-catalyzed introduction of a variety of functional groups.

Scheme 11



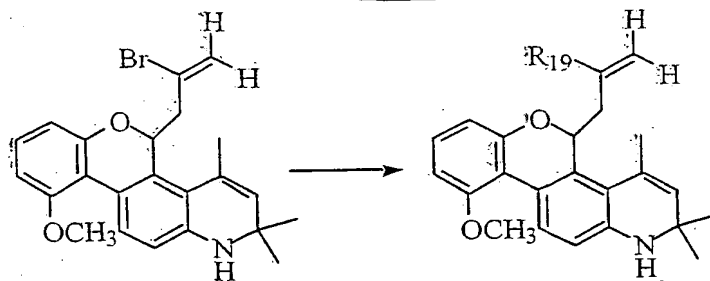
As shown in Scheme 11, cores bearing phenolic hydroxyl functionality were either dehydroxylated (as shown for Core 2), acetylated, or alkylated by transformations well-known in the art. See Larock, "Comprehensive Organic Transformations. A Guide to Functional Group Preparations," VCH Publishers, New York (1989), hereby incorporated by reference.

Scheme 12



Scheme 12 shows the introduction of the substituted cyclohexenyl group by Lewis acid catalyzed addition of the tert-butyldimethylsilyl-protected enol ether to the C-5 position of Example 2B. Once introduced, the diastereomers and rearrangement products were separated, and the alkoxycarbonyl group was optionally reduced to a hydroxyalkyl group.

Scheme 13

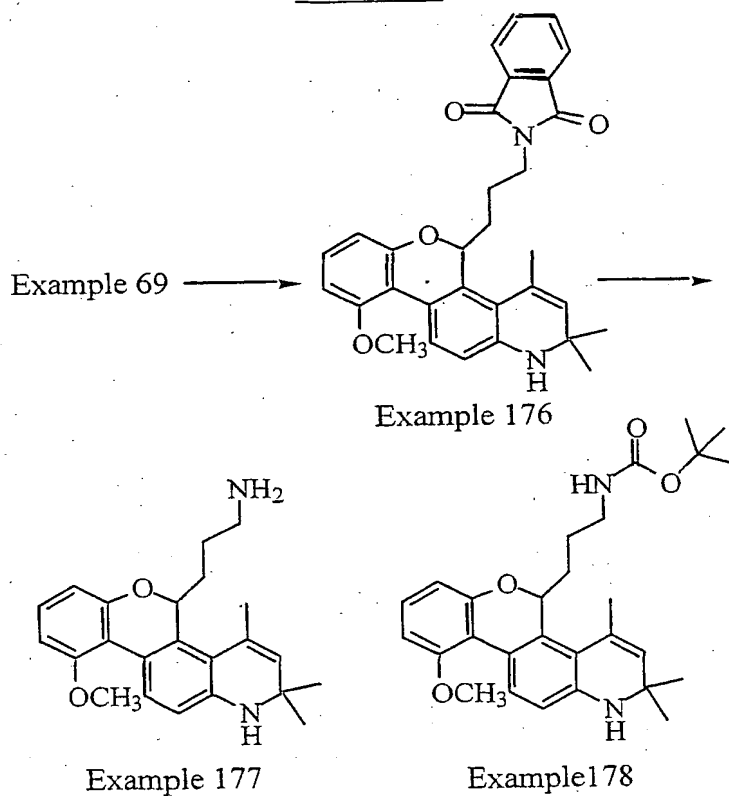


Example 147

Examples 171, 172 and 173

As shown in Scheme 13, the vinylic bromide group of compounds such as Example 147 were further derivatized at the brominated position(s) to provide a number of R<sub>19</sub> substituents by transition metal-catalyzed introduction of a variety of functional groups such as those described in Scheme 10.

Scheme 14

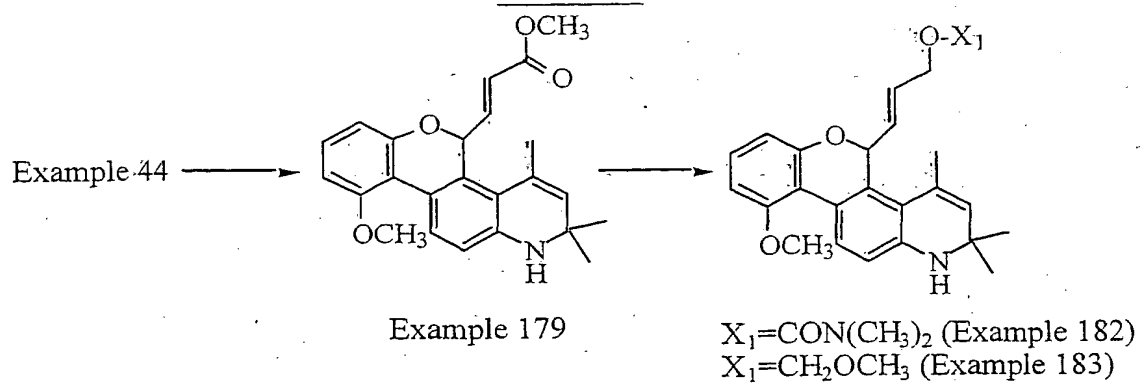


Example 177

Example 178

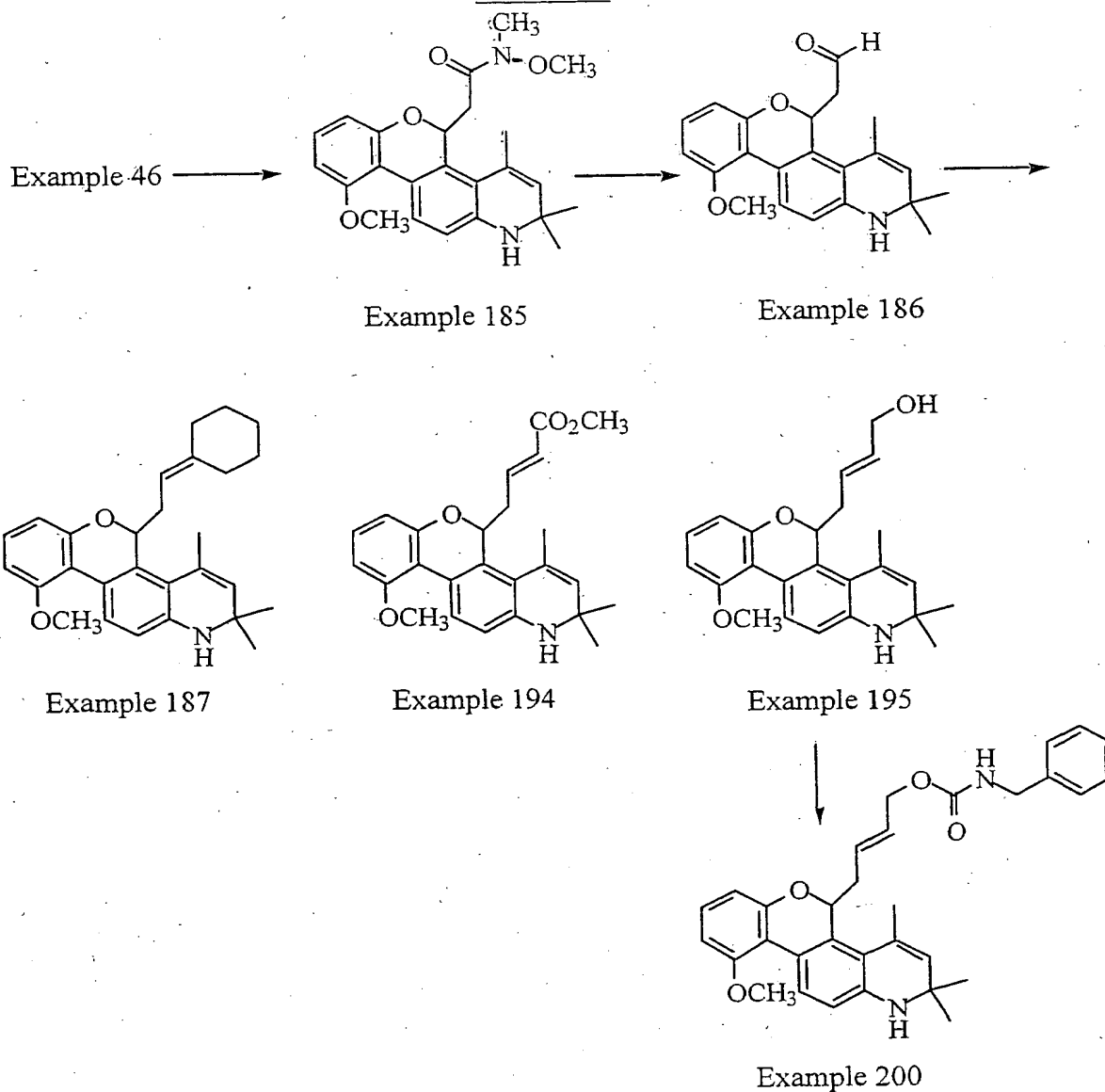
As shown in Scheme 14, Mitsunobu introduction of phthalimide to Example 69 and removal of the imide group with hydrazine provided alkylamino Example 177 which was further derivatized to Example 178 by treatment with di(tert-butyl)dicarbonate.

Scheme 15



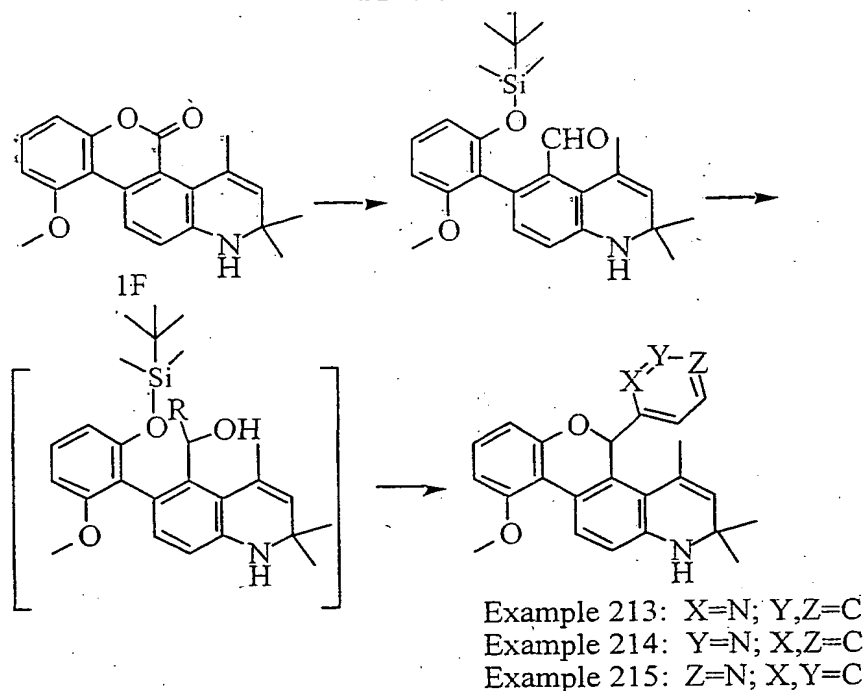
As shown in Scheme 15, elaboration of the C-5 nitrile of Example 44 to the  $\alpha,\beta$ -unsaturated ester Example 179 followed by selective reduction of the alkoxy carbonyl group to the alkenyl alcohol ( $X_1$  is H) provided precursors for carbamates and methoxymethyl ethers Examples 182 and 183, respectively.

Scheme 16



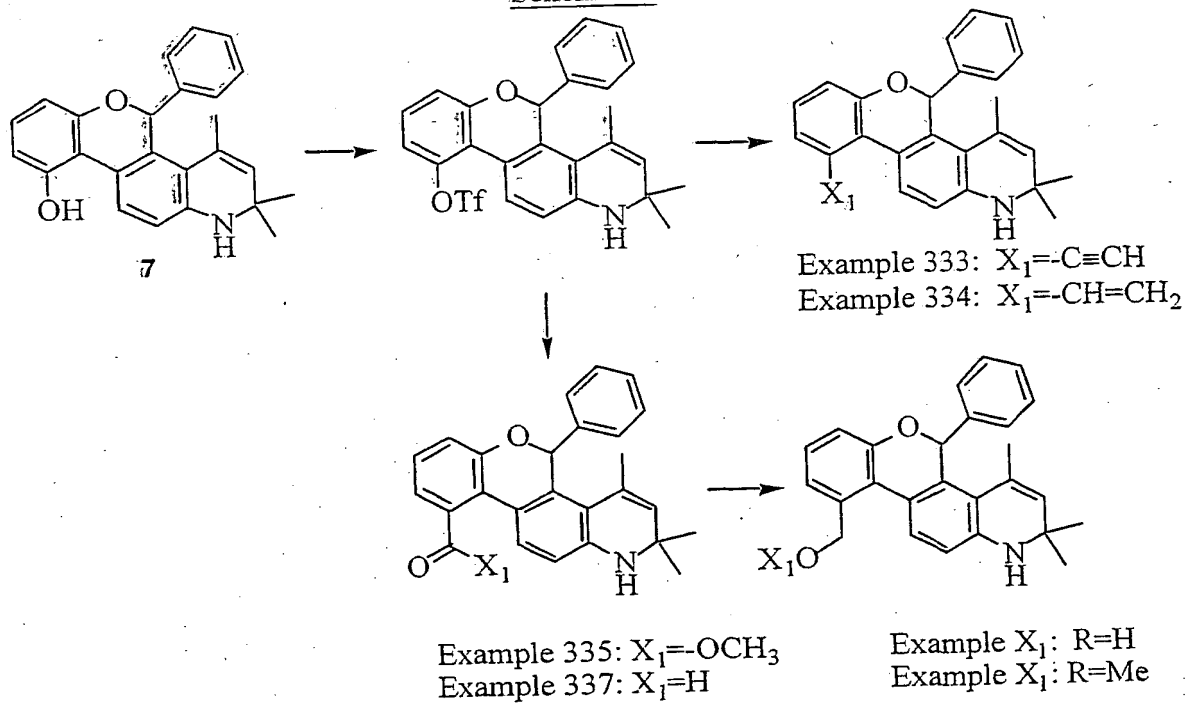
As shown in Scheme 16, conversion of ester Example 46 to its Weinreb amide derivative Example 185 and subsequent reduction to aldehyde Example 186 provided precursors for alkene Examples 187, 194, 195, and 200 by treatment of the aldehydes with a number of commercially available Wittig or Horner-Wadsworth-Emmons reagents.

Scheme 17

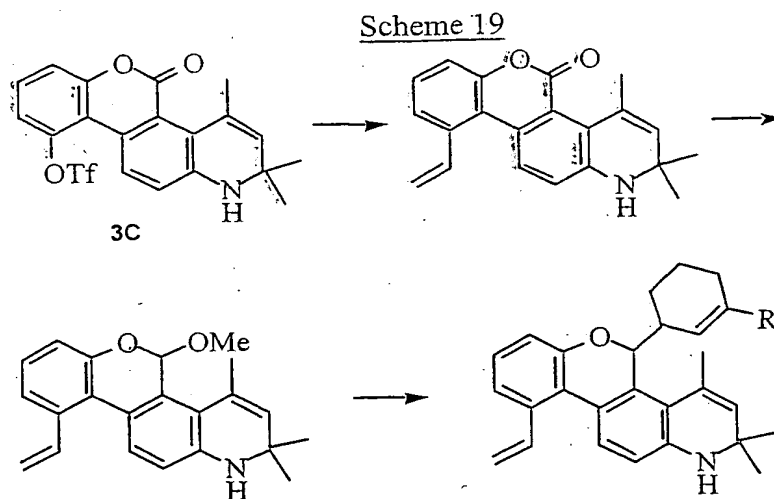


As shown in Scheme 17, Example 1F was converted to a ring-opened aldehyde using a two-step sequence involving treatment with a reducing agent such as diisobutylaluminum hydride in an aprotic solvent such as dichloromethane followed by treatment with a silylating reagent such as *tert*-butyldimethylsilyl chloride in the presence of a base such as potassium *tert*-butoxide. Addition of organolithium reagents such as lithiopyridines to the aldehyde produced benzylic alcohols (R=pyridyl) which could then be converted to analogs such as Examples 213-215 using a two-step sequence comprising removal of the silicon group with reagents such as tetrabutylammonium fluoride and subsequent cyclization using reagent combinations such as triethylphosphine and 1,1'-(azodicarbonyl)dipiperidine.

Scheme 18

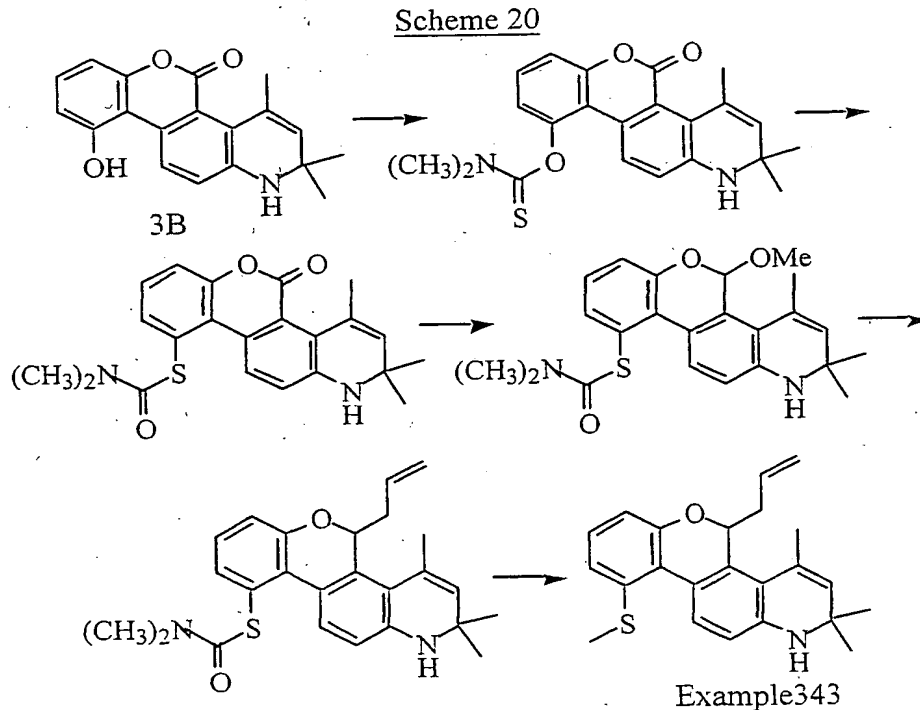


As shown in Scheme 18, Example 7 was converted to the triflate derivative with reagents such as trifluoromethanesulfonic anhydride, then derivatized at the C-10 position using the methods described in Scheme 3. Reduction of Example 335 with reagents such as diisobutylaluminum hydride provided Example 336. Treatment of Example 336 with oxidizing reagents such as tetrapropylammonium perruthenate afforded Example 337. Alkylation of Example 336 could be accomplished with reagents such as iodomethane in the presence of a base such as potassium bis(trimethylsilyl)amide to provide analogs such as Example 338.



Example 340: R=H  
Example 341: R=Me

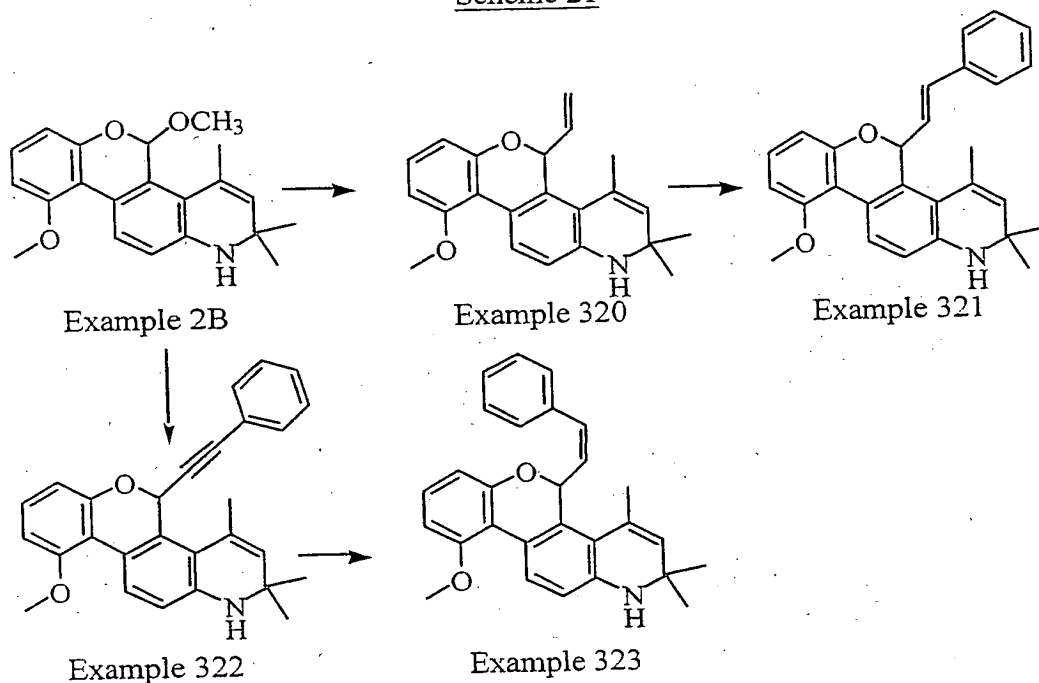
As shown in Scheme 19, triflate 3C was also converted to a C-10 vinyl derivative Example 339 and subsequently to its methyl acetal using the methods described in Schemes 3 and 2, respectively. The acetal was treated with nucleophiles such as 3-(trimethylsilyl)cyclohexene or 3-(dimethylphenylsilyl)-3-methylcyclohexene in the presence of a Lewis acid such as boron trifluoride etherate to provide analogs such as Examples 340 and 341, respectively.



Introduction of sulfur at C-10 position of Example 3B is shown in Scheme 20. Example 3B was treated with reagents such as dimethylcarbamoyl chloride to give a

thionocarbamate which underwent thermal rearrangement to provide the sulfur-carbon bond at C-10. The allyl group at C-5 was introduced as described in Scheme 2. Hydrolysis with a strong base such as potassium hydroxide and alkylation of sulfur with electrophiles such as iodomethane in the presence of a base such as cesium carbonate provided analogs bearing thioalkoxy functionality at C-10, such as Example 343.

Scheme 21



A route to make Examples 320-323 is shown in Scheme 21. Example 2B was treated with nucleophiles such as tributylvinyltin in the presence of Lewis acids such as boron trifluoride diethyl etherate to provide Example 320 which was then coupled with aryl halides such as iodobenzene in the presence of catalysts such as palladium (II) acetate to provide trans isomer Example 321. The Lewis acid/methyl acetal complex was also condensed with tributylphenylacetylenyltin to provide Example 322 which was then partially hydrogenated in the presence of catalysts such as palladium on BaSO<sub>4</sub> to provide cis isomer Example 323.

It is understood from the preceding schemes and the following examples that the substituents R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>16</sub>, R<sub>16'</sub>, R<sub>17</sub>, R<sub>18</sub>, R<sub>18'</sub>, Y, R<sub>2</sub>, and L<sub>2</sub> can be determined by selection of the appropriate commercially available or known starting materials (e.g., substituted methoxybenzenes) or introduced synthetically by known chemical methods such as those disclosed in Larock, "Comprehensive Organic Transformations. A Guide to Functional Group Preparations," VCH Publishers, New York (1989), hereby incorporated by reference.

Also, it will be appreciated by one skilled in the art that selective protection and deprotection steps depending on the nature of R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>16</sub>, R<sub>16'</sub>, R<sub>17</sub>, R<sub>18</sub>, R<sub>18'</sub>, Y, R<sub>2</sub>, and L<sub>2</sub> can be carried out in varying order or number of steps to successfully complete the synthetic sequences. Commonly used protecting groups are disclosed in Greene, "Protective Groups In Organic Synthesis," John Wiley & Sons, New York (1981), hereby incorporated by reference.

Example 1

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinoline 1H-[1]benzopyrano[3,4-f]quinoline

5

Example 1A

A solution of 1,3-dimethoxybenzene (33.2 g, 240 mmol) in hexanes (20 mL) at -20 °C was treated sequentially with n-butyllithium (100 mL of a 2.4 M solution in hexanes, 240 mmol) and N,N,N',N'-tetramethylethylenediamine (1.81 mL, 12 mmol), stirred at 23 °C for 1.5 hours, cooled to -78 °C, treated with triisopropylborate (60.9 mL, 264 mmol) in diethyl ether (60 mL) over 1.5 hours with additional diethyl ether (150 mL) added to maintain stirring, stirred at 23 °C for 2 hours, poured into ice (150 mL) and 3M HCl (150 mL), and extracted with ethyl acetate. The extract was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated, during which a white solid precipitated from solution. The solid was collected by filtration and washed with hexanes to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 200 (M+NH<sub>4</sub>)<sup>+</sup>.

Example 1B

A mixture of Example 1A, methyl 5-nitro-2-bromobenzoate (25.8 g, 99.2 mmol), (21.7 g, 119 mmol), cesium carbonate (97.1 g, 298 mmol), and dichlorobis-(triphenylphosphine)palladium(II) (3.5 g, 5.0 mmol) in DMF (300 mL) was stirred for 24 hours at 80 °C, cooled to 23 °C, treated with water (600 mL), and extracted with ethyl acetate (800 mL). The extract was dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated, during which a light yellow solid precipitated from solution. The mixture was placed in a freezer (-20 °C) for 2 hours then filtered to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 318 (M+H)<sup>+</sup> and 335 (M+NH<sub>4</sub>)<sup>+</sup>.

Example 1C

A solution of Example 1B (11.1 g, 35.1 mmol) in dichloromethane (60 mL) at -78 °C was treated with boron tribromide (25.0 g, 99.8 mmol), warmed to 23 °C for 1 hour, re-cooled to -78 °C, and treated with methanol (100 mL). The mixture was warmed to 0 °C, and the precipitate was collected by filtration and recrystallized from methanol to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 275 (M+NH<sub>4</sub>)<sup>+</sup>.

Example 1D

A mixture of Example 1C (10.7 g, 41.6 mmol) and  $\text{Cs}_2\text{CO}_3$  (20.0 g, 61.4 mmol) in DMF (130 mL) at 23 °C was treated dropwise with methyl iodide (22.8 g, 161 mmol), stirred for 4 hours, treated with water, and extracted with 1:1 ethyl acetate/hexane. The extract was concentrated, and the resulting solid was filtered, washed with water (100 mL), and dried under vacuum to provide the desired compound.  
MS (DCI/ $\text{NH}_3$ ) m/z 289 ( $\text{M}+\text{NH}_4$ )<sup>+</sup>.

#### Example 1E

A suspension of Example 1D (11.2 g, 41.3 mmol) in dioxane (400 mL) at 23 °C was treated with 10% palladium on carbon (580 mg), heated at 65 °C, treated with hydrogen, stirred under atmospheric pressure for 60 hours, filtered through powdered sea shells (Celite®) while hot, and concentrated during which a precipitate formed. The product was filtered and dried under vacuum to provide the desired compound. Concentration of the mother liquor to half of its original volume afforded a second crop of desired compound.  
MS (DCI/ $\text{NH}_3$ ) m/z 242 ( $\text{M}+\text{H}$ )<sup>+</sup> and 259 ( $\text{M}+\text{NH}_4$ )<sup>+</sup>.

#### Example 1F

A solution of Example 1E (4.0 g, 16.6 mmol) and iodine (1.7 g, 6.64 mmol) in acetone (380 mL) in a 1L sealed ACE glass high pressure vessel at 105 °C was stirred for 48 hours, cooled to room temperature, and concentrated. The residue was purified by flash chromatography on silica gel with 0 to 12% ethyl acetate/hexanes to provide the desired compound.  
MS (DCI/ $\text{NH}_3$ ) m/z 322 ( $\text{M}+\text{H}$ )<sup>+</sup>.

#### Example 1G

A solution of Example 1F (1.02 g, 3.18 mmol) in THF (20 mL) at -78 °C was treated with a solution of phenyllithium (10.9 mL, 19.6 mmol) in cyclohexanes/diethyl ether, warmed to -50 °C, stirred for 2 hours, treated with saturated  $\text{NH}_4\text{Cl}$ , warmed to 25 °C, and extracted with ethyl acetate. The extract was dried ( $\text{Na}_2\text{SO}_4$ ), filtered, and concentrated. The residue was purified by flash chromatography on silica gel with 20% ethyl acetate/hexanes to provide the desired compound.  
MS (DCI/ $\text{NH}_3$ ) m/z 400 ( $\text{M}+\text{H}$ )<sup>+</sup>.

#### Example 1

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinoline 1H-[1]benzopyrano[3,4-f]quinoline

A solution of Example 1G (0.67 g, 1.67 mmol) in dichloromethane (30 mL) at -78 °C was treated with triethylsilane (2.91 g, 25.05 mmol) and BF<sub>3</sub>·OEt<sub>2</sub> (0.95 g, 6.68 mmol), warmed to room temperature, stirred for 16 hours, and treated with saturated NaHCO<sub>3</sub>. The organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated. The residue was purified by flash chromatography on silica gel with 5% ethyl acetate/hexanes to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 384 (M+H)<sup>+</sup>;

<sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) δ 8.00 (d, 1H), 7.19 (m, 5H), 6.9 (dd, 1H), 6.76 (s, 1H), 6.69 (dd, 1H), 6.55 (d, 1H), 6.43 (d, 1H), 6.2 (s, 1H), 5.38 (s, 1H), 3.8 (s, 3H), 1.83 (s, 3H), 1.22 (s, 3H), 1.14 (s, 3H);

Anal. calcd for C<sub>26</sub>H<sub>25</sub>NO<sub>2</sub>: C, 81.42; H, 6.58; N, 3.65. Found C, 81.28; H, 6.30; N, 3.47.

#### Example 2

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline

#### Example 2A

A solution of Example 1F (6.65 g, 20.69 mmol) in dichloromethane (500 mL) at -78 °C was treated dropwise with 1M diisobutylaluminum hydride in hexanes (47.6 mL, 47.6 mmol), stirred for 2 hours, treated sequentially with saturated aqueous sodium potassium tartrate (300 mL) and ethyl acetate (600 mL), and stirred vigorously for 4 hours. The extract was washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 306 (M-OH)<sup>+</sup>.

#### Example 2B

A solution of Example 2A (4.20 g, 12.99 mmol) in methanol (150 mL) at 0° C was treated with p-toluenesulfonic acid·H<sub>2</sub>O (1.2 g, 20 wt %), stirred for 30 minutes, stirred at room temperature for 1 hour, cooled to 0 °C for 30 minutes, and filtered. The solid was rinsed with hexanes and dried under vacuum to provide the desired compound. The filtrate was poured into saturated NaHCO<sub>3</sub> and extracted with ethyl acetate. The extract was washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated. The residue was purified by flash chromatography on silica gel with 10-20% ethyl acetate/hexanes to provide additional desired compound.

MS (DCI/NH<sub>3</sub>) m/z 306 (M-OCH<sub>3</sub>)<sup>+</sup>.

#### Example 2

2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline

A solution of Example 2B (2.50 g, 7.41 mmol) in dichloromethane (225 mL) was treated with allyltrimethylsilane (4.0 mL, 25.2 mmol), cooled to -78 °C, treated dropwise with BF<sub>3</sub>·OEt<sub>2</sub> (3.1 mL, 25.2 mmol), stirred for 15 minutes at -78 °C, warmed to 0 °C for 30 minutes, treated with saturated NaHCO<sub>3</sub>, and extracted with ethyl acetate. The extract was washed with brine, dried (MgSO<sub>4</sub>), filtered, and concentrated. The residue was purified by flash chromatography on silica gel with 5-20% ethyl acetate/hexanes to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 348 (M+H)<sup>+</sup>;

<sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) δ 7.96 (d, 1H), 7.07 (t, 1H), 6.71 (d, 1H), 6.60 (d, 1H), 6.52 (d, 1H), 6.12 (br s, 1H), 5.82 (m, 1H), 5.76 (dd, 1H), 5.44 (br s, 1H), 5.01 (m, 2H), 3.86 (s, 3H), 2.44 (m, 1H), 2.20 (m, 1H), 2.16 (s, 3H), 1.17 (s, 3H), 1.16 (s, 3H);

Anal. calcd for C<sub>23</sub>H<sub>25</sub>NO<sub>2</sub>: C, 79.51; H, 7.25; N, 4.03. Found: C, 79.35; H, 7.30; N, 3.89.

Example 3 Claim

2,5-dihydro-2,2,4,N-tetramethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinolin-10-amine

Example 3A

A solution of Example 1C was processed as in Example 1E to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 227 (M+H)<sup>+</sup>.

Example 3B

A solution of Example 3A was processed according to the procedure in Example 1F to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 308 (M+H)<sup>+</sup>.

Example 3C

A solution of Example 3B (1.38 g, 4.49 mmol), triethylamine (1.92 mL, 13.77 mmol) and 4-dimethylaminopyridine (100 mg) in dichloromethane (50 mL) at -78°C, was treated dropwise with trifluoromethanesulfonic anhydride (1.39 g, 4.94 mmol); stirred 30 minutes at -78° C, warmed slowly to room temperature over 1.5 hours, poured into saturated NH<sub>4</sub>Cl, and extracted with ethyl acetate. The extract was washed with water, dried (MgSO<sub>4</sub>), filtered, and concentrated. The residue was purified by flash

chromatography on silica gel with 10% ethyl acetate/hexanes to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 440 (M+H)<sup>+</sup>.

#### Example 3D

Example 3C was processed according to the procedures in examples 2A, 2B and 2 to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 466 (M+H)<sup>+</sup>.

#### Example 3

##### 2,5-dihydro-2,2,4,N-tetramethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinolin-10-amine

A solution of Example 3D (0.165 g, 0.36 mmol), palladium(II) acetate (0.0016 g, 0.007 mmol), (S)-(-)-2,2'-bis(phenylphosphino)-1,1'-binaphthyl (0.0055, 0.008 mmol), sodium tert-butoxide (0.051 g, 0.53 mmol), methylamine (0.44 mL of a 2.0M solution in THF, 0.88 mmol) in toluene (0.5 mL) was heated at 90 °C for 4 hours in a sealed ACE-glass high pressure vessel, cooled to 0 °C, diluted with ethyl acetate (5 mL), and washed with 0.5M HCl. The organic extract was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated.

The residue was purified by flash chromatography on silica gel with 5-12% ethyl acetate/hexanes to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 347 (M+H)<sup>+</sup>;

<sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>)  $\delta$  7.83 (d, 1H), 6.94 (dd, 1H), 6.62 (d, 1H), 6.28 (dd, 1H), 6.25 (dd, 1H), 6.05 (d, 1H), 5.86-5.74 (m, 2H), 5.67 (dd, 1H), 5.45 (s, 1H), 5.40 (q, 1H), 5.03 (dd, 1H), 4.98 (dd, 1H), 2.72 (d, 3H), 2.16 (s, 3H), 1.17, (s, 3H), 1.15 (s, 3H); HRMS m/z calcd for C<sub>23</sub>H<sub>26</sub>N<sub>2</sub>O: 346.2045 (M+H)<sup>+</sup>. Found: 346.2049.

#### Example 4

##### methyl 2,5-dihydro-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline-10-carboxylate

A solution of Example 3D (263 mg, 0.565 mmol), triethylamine (0.10 mL, 0.717 mmol), 1,3-bis(diphenylphosphino)propane (26 mg, 0.063 mmol) and DMSO (1.5 mL) in methanol (8 mL) was treated with palladium acetate (12.7 mg, 0.056 mmol), saturated with carbon monoxide, stirred under carbon monoxide (1 atm) for 20 minutes, heated at 65 °C for 3 hours, cooled, diluted with ethyl acetate (100 mL), and filtered. The filtrate was washed with brine, dried (MgSO<sub>4</sub>), filtered, and concentrated. The residue was purified by flash chromatography on silica gel with 5-10% ethyl acetate/hexanes to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 376 (M+H)<sup>+</sup>;

$^1\text{H}$  NMR  $\delta$  7.19 (m, 2H), 7.03 (dd, 1H), 6.78 (d, 1H), 6.60 (d, 1H), 6.30 (m, 1H), 5.85 (m, 2H), 5.46 (m, 1H), 5.05 (dm, 1H), 4.98 (dm, 1H), 3.77 (s, 3H), 2.30 (m, 2H), 2.19 (d, 3H), 1.21 (s, 3H), 1.15 (s, 3H);  
HRMS  $m/z$  calcd for  $\text{C}_{24}\text{H}_{25}\text{NO}_3$ : 375.1834 ( $\text{M}+\text{H}$ ) $^+$ . Found: 375.1841.

#### Example 5

##### 10-ethenyl-2,5-dihydro-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline

A solution of Example 3D (103 mg, 0.221 mmol) and (1,3-bis(diphenylphosphino)ferrocene)palladium (II) chloride-dichloromethane (22 mg, 0.027 mmol) in 1-methyl-2-pyrrolidinone (2 mL) was treated with vinyl tributylstannane (0.110 mL, 119 mg, 0.376 mmol), heated at 65 °C for 24 hours, cooled to room temperature, treated with saturated KF, and extracted with ethyl acetate. The extract was washed with brine, dried ( $\text{MgSO}_4$ ), filtered, and concentrated. The residue was purified by flash chromatography on silica gel with 5% ethyl acetate/hexanes to provide the desired compound.

MS (DCI/ $\text{NH}_3$ )  $m/z$  344 ( $\text{M}+\text{H}$ ) $^+$ ;

$^1\text{H}$  NMR  $\delta$  7.22 (d, 1H), 7.15 (m, 2H), 6.99 (dd, 1H), 6.83 (dd, 1H), 6.63 (d, 1H), 6.23 (m, 1H), 5.87 (ddm, 1H), 5.73 (dd, 1H), 5.76 (dd, 1H), 5.47 (m, 1H), 5.33 (dd, 1H), 5.03 (dd, 1H), 4.98 (dm, 1H), 3.77 (s, 3H), 2.44 (m, 1H), 2.28 (m, 1H), 2.18 (d, 3H), 1.21 (s, 3H), 1.15 (s, 3H);

HRMS  $m/z$  calcd for  $\text{C}_{24}\text{H}_{26}\text{NO}$ : 344.2014 ( $\text{M}+\text{H}$ ) $^+$ . Found: 344.2011

#### Example 6

##### 10-ethynyl-2,5-dihydro-10-methoxy-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline

#### Example 6A

A solution of Example 3D (25 mg, 0.054 mmol), tetra-*n*-butylammonium iodide (40 mg, 0.108 mmol), bis(triphenylphosphine)palladium chloride (7.0 mg, 0.010 mmol), copper(I) iodide (3.8 mg, 0.020 mmol) and triethylamine (0.15 mL, 0.717 mmol) in DMF (0.75 mL) was treated with trimethylsilylacetylene (174 mg, 1.76 mmol), heated at 55 °C for 3 hours, diluted with ethyl acetate (20 mL), and filtered. The filtrate was washed with saturated  $\text{NH}_4\text{Cl}$ , and the aqueous layer was extracted with ethyl acetate. The combined extracts were dried ( $\text{MgSO}_4$ ), filtered, and concentrated. The residue was applied to a 10 x 20 cm, 0.25 mm silica gel TLC plate and eluted twice with 10% ethyl acetate/hexane. Extraction of the silica gel with ethyl acetate provided the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 414 (M+H)<sup>+</sup>;

<sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>)  $\delta$  8.36 (d, 1H), 7.07 (m, 2H), 6.90 (dd, 1H), 6.60 (d, 1H), 6.34 (m, 1H), 5.80 (m, 2H), 5.46 (m, 1H), 5.04 (dm, 1H), 4.97 (dm, 1H), 2.35 (m, 1H), 2.26 (m, 1H), 2.17 (d, 3H), 1.18 (s, 3H), 1.17 (s, 3H), 0.26 (s, 9H).

#### Example 6

##### 10-ethynyl-2,5-dihydro-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline

A solution of Example 6A in THF (2.5 mL) was treated sequentially with glacial acetic acid (0.005 mL) and 1M tetra-n-butylammonium fluoride in THF (0.050 mL, 0.050 mmol), stirred at room temperature for 18 hours, and purified according to the procedure in Example 6A to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 342 (M+H)<sup>+</sup>;

<sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>)  $\delta$  8.27 (dd, 1H), 7.15 (t, 1H), 7.07 (d, 1H), 6.91 (dm, 1H), 6.62 (d, 1H), 6.34 (m, 1H), 5.80 (m, 1H), 5.46 (m, 1H), 5.03 (dm, 1H), 4.98 (dm, 1H), 4.41 (s, 1H), 2.44 (m, 2H), 2.17 (s, 3H), 1.18 (s, 6H);

HRMS calcd m/z for C<sub>24</sub>H<sub>23</sub>NO: 341.1780 (M+H)<sup>+</sup>. Found: 341.1788.

#### Example 7

##### 2,5-dihydro-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinolin-10-ol

#### Example 7A

A solution of Example 3B (569 mg, 1.85 mmol) in DMF (8 mL) at 23 °C was treated sequentially with imidazole (379 mg, 5.55 mmol) and t-butyldimethylsilyl chloride (418 mg, 2.78 mmol), stirred for 3 hours, poured into water, and extracted with 2:1 hexane/ethyl acetate (22 mL). The extract was washed with water and brine, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated. The residue was purified by flash chromatography on silica gel with 25% ethyl acetate/hexanes to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 422 (M+H)<sup>+</sup>.

#### Example 7B

Example 7A was processed as in examples 1G and 1 to provide the desired compound.

#### Example 7

##### 2,5-dihydro-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinolin-10-ol

A solution of Example 7B (0.90 g, 1.87 mmol) in THF (12 mL) at 0 °C was treated with 1M tetra-n-butylammonium fluoride in THF (3.37 mL, 3.37 mmol), warmed

to 23 °C with over 1 hour, treated with water, and extracted with ethyl acetate. The extract was washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated. The residue was purified by flash chromatography on silica gel with 10-30% ethyl acetate/hexanes to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 370 (M+H)<sup>+</sup>;

<sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) □ 9.63 (s, 1H), 9.16 (d, 1H), 7.13-7.24 (m, 5H), 6.74 (s, 1H), 6.70 (d, 1H), 6.8 (d, 1H), 6.39 (dd, 1H), 6.26 (dd, 1H), 6.11 (d, 1H), 5.37 (s, 1H), 1.85 (d, 3H), 1.22 (s, 3H), 1.11 (s, 3H);

HRMS calcd m/z for C<sub>25</sub>H<sub>23</sub>NO<sub>2</sub>: 369.1729 (M+H)<sup>+</sup>. Found 369.1736.

#### Example 8

10-(difluoromethoxy)-2,5-dihydro-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline

#### Example 8A

A solution of Example 3B (1.11 g, 3.6 mmol) in DMF (10 mL) at 0 °C was treated sequentially with sodium t-butoxide (0.38 g, 3.6 mmol) and bromodifluoromethane (10 mL), stirred at 0 °C for 6 hours, warmed to room temperature for 1 hour, treated with saturated NaHCO<sub>3</sub>, and extracted with ethyl acetate. The extract was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated. The residue was purified by flash chromatography on silica gel with 5% ethyl acetate/hexanes to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 436 (M+H)<sup>+</sup>.

#### Example 8

10-(difluoromethoxy)-2,5-dihydro-2,2,4-trimethyl-5-(2-propenyl)-1H-[1]benzopyrano[3,4-f]quinoline

Example 8A was processed as in examples 2B and 2 to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 384 (M+H)<sup>+</sup>;

<sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) □ 7.75 (d, 1H), 7.20 (t, 1H), 7.15 (t, 1H), 6.83 (dd, 1H), 6.81 (dd, 1H), 6.63 (d, 1H), 6.28 (s, 1H), 5.89-5.75 (m, 2H), 5.46 (s, 1H), 5.04 (dd, 1H), 4.96 (dd, 1H), 2.48-2.40 (m, 1H), 2.29-2.20 (m, 1H), 2.18 (s, 3H), 1.17 (s, 6H);

HRMS calcd for C<sub>23</sub>H<sub>23</sub>F<sub>2</sub>NO<sub>2</sub>: 383.1697 (M+H)<sup>+</sup>. Found 383.1693.

#### Example 9

10-ethoxy-2,5-dihydro-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinoline

Example 9A

A solution of Example 3B (28 mg, .09 mmol) in DMF (1.0 mL) at 0 °C was treated with sodium hydride (2.4 mg of a 60% dispersion in mineral oil, 0.01 mmol), stirred for 1 hour, treated with ethyl bromide (20 mg, .182 mmol), stirred for 30 minutes at room temperature, treated with saturated NaHCO<sub>3</sub>, and extracted with ethyl acetate. The extract was dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated. The residue was purified by flash chromatography on silica gel with 5% ethyl acetate/hexanes to provide the desired compound.

Example 910-ethoxy-2,5-dihydro-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinoline

Example 9A was processed as in examples 1G and 1I to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 398 (M+H)<sup>+</sup>;

<sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) □ 8.09 (d, 1H), 7.20-7.15 (m, 5H), 6.78 (dd, 2H), 6.77 (s, 1H), 6.69 (d, 1H), 6.53 (dd, 1H), 6.43 (dd, 1H), 6.18 (d, 1H), 5.39 (d, 1H), 3.99-4.06 (m, 1H), 1.85 (d, 3H), 1.38 (t, 3H), 1.22 (s, 3H), 1.16 (s, 3H);

HRMS calcd m/z for C<sub>27</sub>H<sub>27</sub>NO<sub>2</sub>: 397.2042 (M+H)<sup>+</sup>. Found 397.2034.

Example 102,5-dihydro-2,2,4-trimethyl-5-phenyl-1H-[1]benzopyrano[3,4-f]quinoline-10-ol acetate (ester)

A solution of Example 7 (20 mg, 0.05 mmol) in pyridine (1 mL) at 0 °C was treated with acetic anhydride (0.1 mL, 1.05 mmol), stirred at room temperature 14 hours, and concentrated. The residue was purified by flash chromatography on silica gel with 20% ethyl acetate/hexanes to provide the desired compound.

MS (DCI/NH<sub>3</sub>) m/z 412 (M+H)<sup>+</sup>;

<sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) □ 7.62 (d, 1H), 7.21-7.16 (m, 5H), 6.93 (t, 1H), 6.77 (s, 1H), 6.73 (d, 1H), 6.65 (dd, 1H), 6.62 (dd, 1H), 6.32 (s, 1H), 5.37 (s, 1H), 2.30 (s, 3H), 1.79 (s, 3H), 1.22 (s, 3H), 1.14 (s, 3H);

HRMS calcd m/z for C<sub>27</sub>H<sub>25</sub>NO<sub>3</sub>: 411.1834 (M+H)<sup>+</sup>. Found: 411.1842.

Example 115-(3-bromo-5-methylphenyl)-2,5-dihydro-10-methoxy-2,2,4-trimethyl-1H-[1]benzopyrano[3,4-f]quinoline